THE NEURAL AND PERCEPTUAL MECHANISMS UNDERLYING SPATIAL INTEGRATION

by

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Title: The Neural And Perceptual Mechanisms Underlying Spatial Integration

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DISSERTATION ABSTRACT

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Title: The Neural And Perceptual Mechanisms Underlying Spatial Integration

The visual system integrates information over space to see surfaces, contours and edges. This integration can be described by a divisive normalization framework in which surrounding contextual information normalizes response to a central target. We ran a set of studies examining perceptual illusions with the intention of better understanding the neural mechanisms responsible for how the visual system integrates information over space. We measured surround integration using the Simultaneous Tilt Illusion. In the first study, we determined the extent to which the probability that different surround regions were co-assigned to the same object as the center impacts how much they are integrated. We found that the magnitude of the illusion was a sum of regional surround effects weighted by their dependency to the center. These results are consistent with a system that uses prior experience with natural scene statistics to integrate regions of space. In the second study, we measured the relationship between individual differences in spatial integration and autistic traits. We found no evidence for reduced normalization in people who score high on autistic traits. In the third study, we determined the extent to which arousal modulates spatial integration. Although we did not observe an effect of natural fluctuations in arousal, as indexed by pupil diameter, we observed a reduction in the

magnitude of the illusion following an alerting tone. While more work is still needed to verify this effect, it suggests that we context information less under moderately alert states. We interpret these results in the context of the neural and perceptual mechanisms underlying spatial integration. Specifically, these results seem to indicate that the normalization process is gated by our expectancies about the structure of a scene and by our internal brain state. These results are consistent with a system that uses prior experience with scene statistics to represent patterns more efficiently.

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For my mom, who taught me to be persistent, and my dad, who taught me to be analytical, and my sister, who taught me to be balanced.

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CHAPTER 1: INTRODUCTION

Spatial Integration

Rarely do we observe anything in isolation. And although the visual images that make up a scene can be broken down into a series of small, disjointed lines, our experience of the scene is cohesive. We are able to connect bits of information and separate others to see surfaces, contours, edges and, ultimately, the objects that exist in the world. This requires the visual system to integrate information over space.

We often rely on context to fill in missing information (e.g., occlusion, blind spot, Kanizsa figures, color constancy). Spatially integrating information also allows us to group and segment objects or surfaces as a way to synthesize global structures or disambiguate nearby objects. In order to integrate this information, the visual system compares the response of a single neuron to the response of a group of similar neurons. Neurons in the primary visual cortex are sensitive to edges and are spatially arranged in the cortex based on orientation preference. Because of this orderly representation in the brain, there are some important inferences we can make about orientation-specific spatial integration. Using knowledge of the structure of the visual system combined with data from psychophysical experiments, we can study the underlying processes involved with spatial integration.

In this chapter, I will review and synthesize the literature pertaining to the perceptual and neural basis of orientation-specific spatial integration. I will mostly focus on the spatial aspect of integration but I will occasionally refer to relevant

papers about temporal integration (which use adaptation techniques like the Tilt After Effect; TAE). Within orientation-specific spatial integration, I will focus on surround suppression and surround facilitation effects. I will cover papers that define the perceptual effects of these contextual stimuli and report the theories researchers have established to explain them. I will refer to evidence from single cell recordings and modeling work, which supports (and sometimes contradicts) those theories. Finally, I will also discuss studies of contrast surround suppression and facilitation, since these well-studied effects seem to share some of the same mechanisms as those related to the contrast effects associated with perceived orientation.

Basic Surround Effects

It is often important for the brain to take into account surrounding information when processing a local cue. The classical receptive field (CRF) is an area in the visual field to which a neuron is sensitive (Hubel & Wiesel, 1968). However, response to stimuli in the CRF can be modulated by neighboring neurons when surrounding stimuli are present (e.g., Nelson & Frost, 1978). Therefore, we can define surround effects as the difference in a neuron's response to an optimal stimulus with and without surround information (Albright & Stoner, 2002). From the population level this neural modulation of response will lead to a change in the perception in the local stimulus. Below I will describe the general perceptual and neural effects of contextual stimuli, describe how the contextual stimuli are defined and provide evidence for theories behind the effects.

Perceptual Surround Effects

There are several types of visual stimuli that experimenters use to induce perceptual surround effects. As you will see, each stimulus yields slightly different effects. Therefore, it is important to consider the size, contrast and spatial layout of stimuli in each experiment. In this section, I will report the perceptual effects from several common stimuli used to induce surround effects. Common stimuli include angles created from the intersection of two lines (e.g., Carpenter & Blakemore, 1973; see Figure 1, A), simple flankers (e.g., Kapadia, Ito, Gilbert, & Westheimer, 1995; see Figure 1, B), gabor flankers (e.g., Mizobe, Polat, Pettet, & Kasamatsu, 2001; see Figure 1, C - F), and the Simultaneous Tilt Illusion (STI; e.g., Clifford, 2014; see Figure 1, G). I will also consider different arrangements of flanker stimuli. Flankers that are positioned at the end-zones of the center stimulus (i.e., at the start and end of the center line stimulus) will be referred to as *collinear* (see Figure 1, C-D). Flankers that are positioned to the sides of the center stimulus will be referred to as *lateral* (see Figure 1, E-F). These positions are relative to the orientation of the central stimulus. Regardless of the position of the surrounding stimuli (i.e., full surround, collinear flankers or lateral flankers) the orientation of the surrounds will be specified separately. The orientation will be in reference to the center stimulus orientation. For example, you can have iso-oriented collinear flankers (see Figure 1, C) or orthogonally oriented collinear flankers (see Figure 1, D).

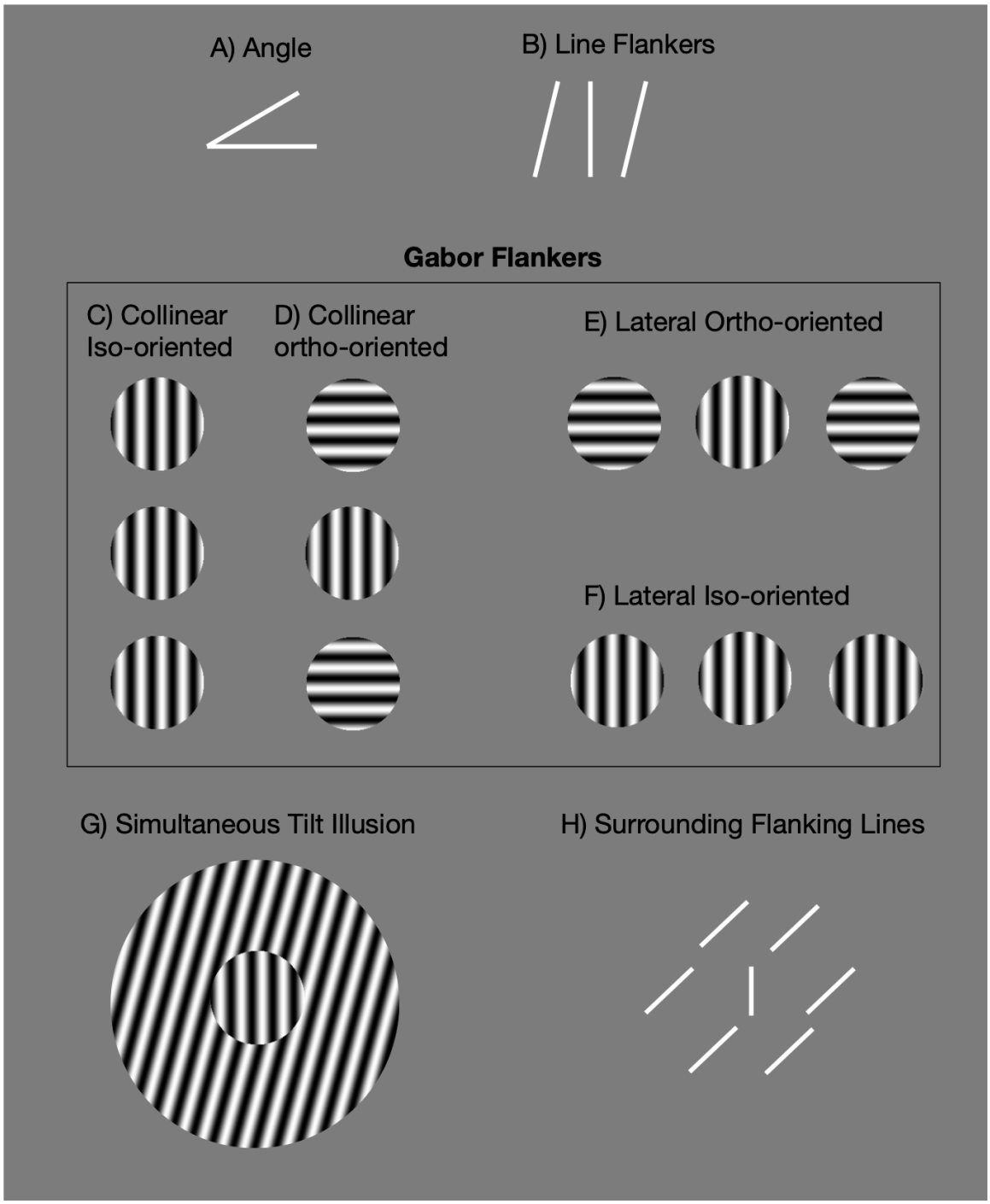

Figure 1. Example contextual stimuli. A) Angle. B) Line flankers. C) Collinearly positioned iso-oriented Gabor flankers. D) Collinearly positioned orthogonally-oriented Gabor flankers. E) Laterally positioned orthogonally-oriented Gabor flankers. F) Laterally positioned iso-oriented Gabor flankers. G) 15 degree Simultaneous Tilt Illusion. H) Surrounding flanking lines. These are not drawn to scale, they are just meant to demonstrate some of the possible arrangements of surround stimuli.

The angular difference between the orientations of the inducing and test stimuli determines the magnitude and direction of the illusion. The surrounding contextual stimuli can induce a *repulsive* shift in perception of a feature of the target. A repulsive shift means that perception is altered so that the target feature appears to be less like the surround. The surrounding contextual stimuli can also induce an *attractive* shift in perception of a target feature. Here, the target feature would be perceived as being more similar to the surround (i.e., perception of the center orientation would be biased in the direction of the surround). The attractive effect is often smaller than the repulsive effect.

Surround orientation effects are well established using the Simultaneous Tilt Illusion, STI (Clifford, 2014; Gibson & Radner, 1937; Westheimer, 1990). The STI is a situation in which a surrounding stimulus biases the perceived orientation of a simultaneously presented central test stimulus (See Figure 2). In the case of the STI, a repulsive effect means that the perceived orientation of the center will be biased in the direction opposite the surround. The strongest repulsive effect happens where the difference between the angle of the center and surround is 15-25 degrees. This is also referred to as a direct tilt illusion. In the case of the STI, the strongest attractive effect occurs when there is a relative difference of 75-80 degrees. This is also referred to as an indirect illusion.

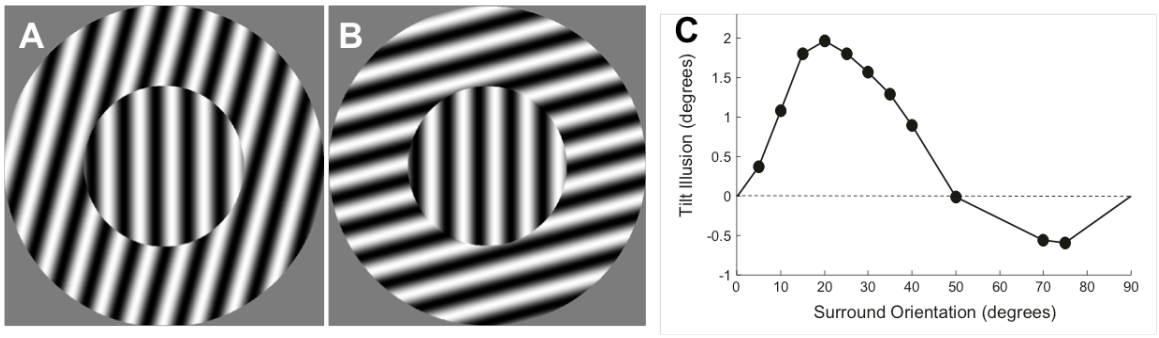

Figure 2. Example of (A) perceptual repulsion and (B) perceptual attraction of an oriented stimulus to the surround. The magnitude of the illusion changes with relative orientation of the center and surround (C, taken from Clifford (2014) Figure 1B).

The tilt after effect (TAE) is similar to the STI, with the main difference being that the contextual stimulus is in the same location as the central stimulus and precedes it in time (Gibson & Radner, 1937). In this early study, the authors tested how exposure to a tilted line would affect subject's perception of the orientation of a subsequent line. They found that when the inducing line angle was less than 45 degrees, the subsequent vertical test line was perceived as being oriented in the opposite direction of the inducing line tilt. When the inducing line angle was 45-90 degrees the vertical test line was perceived as being oriented in the same direction as the inducing line tilt. Although the TAE is not the same as the STI, we can see that there are some similarities in the perceptual response to the two paradigms.

The repulsive tilt effect is present when spatial (STI) or temporal (TAE) inducing stimuli are up to 45 degrees from the orientation of the central or target stimulus when the stimuli are presented centrally (Gibson & Radner, 1937; Westheimer, 1990). However, when stimuli are presented in the periphery this repulsive effect is preserved when the surround stimuli are up to 90 degree

different for the TAE (Muir & Over, 1970) and the STI (Over, Broerse, & Crassini, 1972). This suggests that there is broader orientation tuning in the periphery (Over et al., 1972; see Figure 3, left). Broader tuning would lead to neurons with a wide range of orientation preferences being potentially modulated by the surround. Therefore, the surround could have an effect outside the range it would with a more narrowly tuned response to the center.

Another way to broaden the tuning response to the central stimulus is to increase the orientation bandwidth of the stimuli, rather than using a single orientation. Using STI stimuli that were made up of more natural-looking textures, Goddard, Clifford and Solomon (2008) reproduced a similar pattern of results as the classical STI (see Figure 3, right). The authors also show that the repulsive effect increases when the center orientation bandwidth has a higher standard deviation (i.e., is broader) than the surround. Increasing the bandwidth would broaden the central tuning curve by making more neurons responsive to the different orientations, therefore leaving more neurons susceptible to potential modulation by the surround. It also demonstrates that the general results from the tilt illusion can be applied to stimuli with broadband frequencies and orientations. This is important because stimuli used in the STI are very controlled and not likely to be seen in the real world. Some researchers have proposed doing basic research with stimuli that have statistical properties of natural scenes with the idea that the visual system evolved to be tuned to these statistics (Felsen & Dan, 2005). In fact, one of the main computational models I will discuss later uses regularities in natural scene statistics to predict neural and perceptual STI effects (Schwartz, Sejnowski, &

Dayan, 2009, discussed in the Normalization and Gain Control section). Therefore, it is relevant to consider the difference between how "simple" and more "natural" STI stimuli would affect spatial integration.

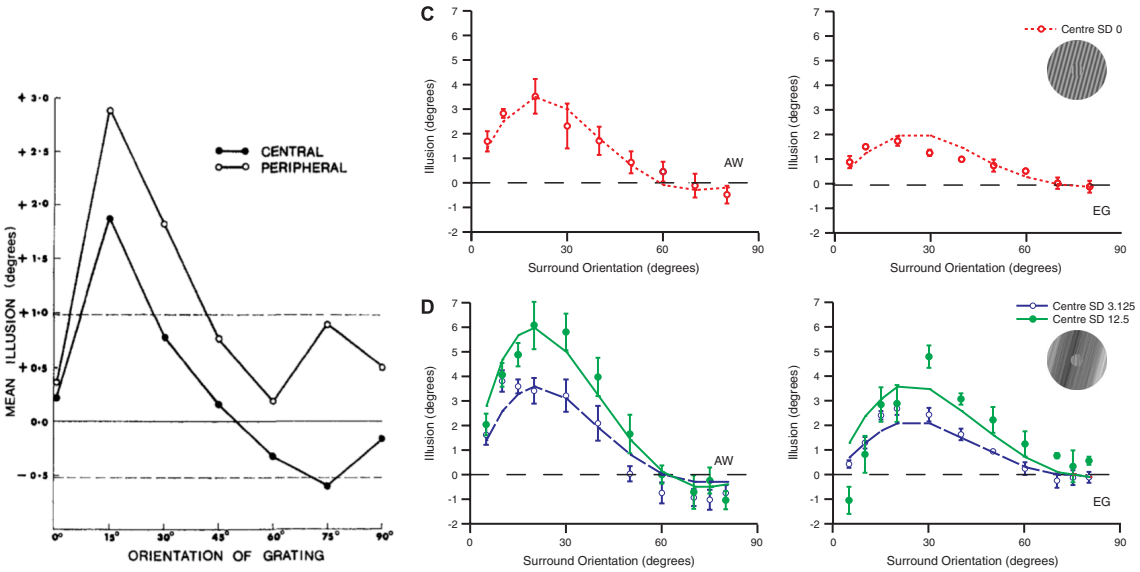

Figure 3. Broader tuning of responses to the central stimulus increases the potential surround effect. Left graph: The repulsive effect of the STI presented peripherally is larger than the repulsive effect of the STI presented centrally (taken from Over, Broerse, & Crassini, 1972). Right set of graphs: The repulsive effect is larger when the central stimulus has a higher standard deviation for orientation bandwidth (taken from Goddard, Clifford & Solomon, 2008).

One advantage to using a stimulus containing flanking lines rather than a full surround is that you can control the geometric position of the inducing contextual stimulus. There is evidence that spatial position of the contextual stimulus will determine the magnitude and direction of the tilt effect (Chen & Tyler, 2008; Coen-Cagli, Dayan & Schwartz, 2012; Kapedia, Westheimer, & Gilbert, 2000; Mizobe et al., 2001; Qiu, Kersten, & Olman, 2013; Schwartz, Sejnowski, & Dayan, 2006). I will

break this down in more detail in the Surround Regions section. For now, I will just present evidence that simple flanking lines can induce the tilt effect.

As shown in Figures 1 and 2, the STI (and TAE) stimuli are typically large high contrast gratings. But orientation effects can be examined with more simple stimuli, like the simple line surrounds used by Westheimer (1990; see Figure 1, H for example). Consistent with the effects of the full STI, Westheimer found that the maximum repulsive effect occurred when the surrounding lines were tilted about 20 degrees away from the orientation of the central line.

The tilt illusion can even occur when there is only one inducing line. In an early study, using angle matching, the authors found that by simply connecting a target line to an inducing line to form an angle, the subjects' perception of the orientation of the lines became biased (Carpenter & Blakemore, 1973). The authors found that participants over estimated the orientation of the target line (i.e., estimated the angle between the two lines as being wider than it actually was) when the inducer was tilted less than 90 degrees, with a peak repulsive effect at 15 degrees. When the inducer was tilted beyond 90 degrees there was a small attractive effect.

This effect is also modulated by the position of the inducing stimuli. Kapadia et al. (2000) demonstrate that two collinear flankers will have an attractive effect on the central line for small orientation differences (less than 10 degrees) and a repulsive effect that is at a maximum for orientation differences between 15-45 degrees. When the flanking lines are positioned lateral to the central line they

induce a repulsive effect up until about 60 degrees difference. Beyond this orientation the effect neutralizes and then becomes attractive.

In summary, perceptual surround effects can be induced using several types of stimuli. In general, the effect is repulsive when the surrounding stimulus orientation is around 15 degrees different from the orientation of the central stimulus. The effect tends to disappear and even become attractive at large orientation differences, around 75 degrees. This attractive effect is much smaller than the magnitude of the repulsive effect. Furthermore, the magnitude and direction of the effect will vary depending on the characteristics of the surround stimulus.

Next I will describe how these perceptual surround effects can be interpreted from a neural perspective, with the perceptual repulsive effect generally related to neural *suppression* and the perceptual attractive effect related to a neural *facilitation*. However, it is important to remember that the overall contextual effect of any stimulus is the summation of suppressive and facilitative neural effects acting on each neuron in the population that is involved in perception of the stimulus. In the remainder of this text, when referring to perceptual effects, I will often refer to the test stimulus as the "center" and the inducing stimulus as the "surround", based on the classic center/surround arrangement of the STI. This terminology is also somewhat analogous to a description of the center/surround layout of a receptive field but, this analogy is only a rough one. Therefore, when I need to be more specific about the definition of a region I will use more specific terms or even refer to the region in the context of the methods used to define it.

Neural surround effects and the classical and extra-classical receptive fields

Originally, scientists thought that a neuron's response to a stimulus in its receptive field was independent of the responses from other neurons (Hartline & Graham, 1932). Later, they began to realize that a neuron's response could be modulated by the responses of other neurons (Allman, Miezin, & McGuinness, 1985; Blakemore & Tobin, 1972; Cavanaugh, Bair and Movshon, 2002; Gilbert & Weisel, 1990; Kapadia et al., 1995; Knierim & van Essen, 1992; Levitt and Lund 1997; Maffei & Fiorentini ,1976; Nelson & Frost, 1978). This led to the distinction between the CRF and the extra-classical receptive field (eCRF, Allman et al., 1985). The CRF became defined as the maximum area in the visual field where a stimulus will directly alter the firing rate of a target neuron. Stimuli in the eCRF (just outside of the CRF and generally 2-5 times larger, Maffei & Fiorentini, 1976) will not directly alter the firing rate of the neuron, but can potentially modulate the neural response to stimuli in the CRF. By this definition, surround integration can only happen when both the CRF and the eCRF are stimulated simultaneously.

Nelson and Frost (1978) demonstrated this effect in the cat visual cortex by presenting flanking lines around a central line. The presence of the surrounding lines lead to a decrease in activity in the neural response to the central line. However, the surround lines alone did not stimulate the recorded neuron. (Blakemore and Tobin, 1972 had shown this in a complex cell before). Furthermore, when a central stimulus increases in size and reaches beyond the CRF it will cause iso-oriented surround suppression (Cavanaugh et al., 2002; Gilbert & Weisel, 1990; Kim & Freeman, 2014; Sceniak, Ringach, Hawken, & Shapley, 1999).

However, defining these receptive field regions experimentally can be tricky because the CRF and eCRF respond differently under different stimulus conditions. For example, it can appear as though the size of the CRF changes with the contrast of the stimulus. There have been several papers that report an increase in CRF size for low contrast stimuli (e.g., Kapadia et al., 1999; Sceniak et al., 1999). In an early study, Sengpiel, Sen and Blakemore (1997) measured a variety of contextual effects on the CRF when the effects of the eCRF were still very much in debate. Most of the neurons showed suppression, but they proposed that there was also a facilitative area in the eCRF. When they presented their stimuli with low contrast centers and iso-oriented surrounds they found that the size of the center summation area increased.

Some researchers suggested that this increase in the CRF for low contrast stimuli is a facilitative response from the surrounding eCRF (Sengpiel et al., 1997; Kim & Freeman, 2014). In contrast, there typically was no effect or a decrease in response from the target neuron (aka a suppressive effect; e.g., Sceniak et al., 1999) when a high contrast stimulus impinged on the eCRF. To account for this, some researchers (Kim & Freeman, 2014; Stemmler, Usher & Niebur, 1995; Somers et al., 1998) have theorized that there are both excitatory and inhibitory connections from the surrounding neurons to the target neuron (see Figure 4). They propose that at low contrasts (or with generally weak stimuli), both the CRF and the eCRF receive weak stimulation. Weak stimulation comes from stimuli that do not optimally stimulate a neural response (e.g., simple flanking lines, orthogonal gabor orientations, or low contrast stimuli). The weak eCRF stimulation causes a small

excitatory signal to be sent to the CRF, therefore increasing the response of the target neuron. According to this hypothesis, the weak stimulation is not enough to trigger the inhibitory connections to the CRF, since these pathways have a higher threshold. But when the stimulus contrast is high and reaches beyond the CRF to the surrounding areas, a strong inhibitory signal is sent to the target neuron that stops the increase in activation or even suppresses it (also see end-stopping; Kapedia et al., 1995).

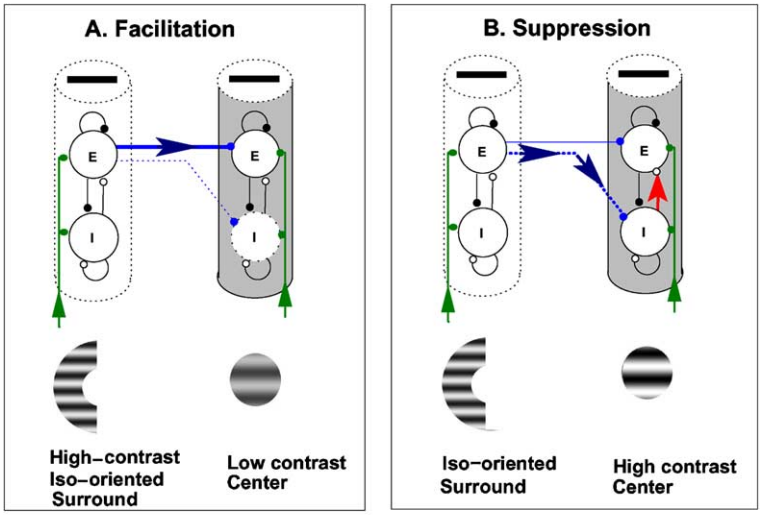

Figure 4. Cartoon of proposed mechanism to account for low contrast facilitation and high contrast suppression. The center stimulus drives local excitatory responses as well as inhibitory interneurons. A) Local inhibitory neurons have a high threshold and do not respond to low contrast stimuli. The excitatory input from the surround is still too weak to activate the inhibitory neurons but it can enhance the excitatory response. B) High contrast center stimuli activate the inhibitory neurons, which saturates the local excitatory response. The surround enhances the activated inhibitory neurons, which then suppress the local excitatory response. Taken from Series, Lorenceau & Fregnac (2003) Figure 4.

In summary, a target neuron's response to a stimulus in the CRF can be modulated by the presence of stimuli in the eCRF. This modulation can have a suppressive or facilitative effect on the target neuron's response. The exact size of

these areas can be difficult to define experimentally because the responses are dependent on the stimulus strength. In particular, it seems that iso-oriented stimuli can facilitate neural response to a weak central stimulus but once the stimulation increases enough to activate the suppressive effects the facilitation neutralizes and becomes suppressive.

How do these neural connections work?

Individual neurons have a preferred orientation to which they respond maximally. At the same time, they have relatively wide tuning functions, meaning that while they respond maximally to a preferred orientation, they also show some response to other orientations. This response decreases with larger angular differences from the preferred orientation. Furthermore, input from the surround can shift the peak response. In this section I will describe the types of connections between neurons that can lead to this shift.

There are three main ways to stimulate the CRF. The first is through feedforward connections (Hubel and Wiesel, 1968). These connections are hierarchical and send information about a stimulus up through successive levels of processing in the visual system. The CRF can also be stimulated by feedback from extrastriate areas (Hupé et al., 1998) or through horizontal connections between nearby cells/hypercolumns (Hirsch and Gilbert, 1991).

Horizontal connections are intrinsic cortical connections, also known as lateral connections. They are the axon transmission between pyramidal cells and can reach up to 8mm across the cortex (Gilbert & Wiesel, 1989; Stettler et al., 2002). These transmissions are also relatively slow because they are unmylinated. Because

of theses physical limitations, the effects driven by horizontal connections are reduced when there is a gap or large distance between the surrounding stimulus and the center (Van Der Smagt, Wehrhahn & Albright, 2005). This phenomenon will be discussed in more detail in the section Timing and Segmentation. Horizontal connections link columns with similar orientation preference (e.g., Gilbert and Wiesel, 1989; Hirsch & Gilbert, 1991; Weliky, Kandler, Fitzpatrick, & Katz, 1995). Although they are orientation selective, their tuning is relatively broad (Gilbert & Wiesel, 1990). These connections can lead to excitation or inhibition (Hirsch & Gilbert, 1991). Glutamate pyramidal neurons are excitatory, but can use interneurons to effectively form inhibitory connections (McGuire, Gilbert, Rivlin, & Wiesel, 1991).

To understand the extent of these lateral interactions, researchers stimulate a hypercolumn with an electrode and then record responses of neighboring neurons. Weliky et al. (1995) showed that the greatest excitatory and inhibitory effects in single neurons occured when neurons that shared the same orientation preference were stimulated. This modulation decreased when the electrodes stimulated a column with a different orientation preference (orthogonal) compared to the recorded neurons. The locations with the greatest inhibition were also the locations where there was the most excitation at low stimulus intensities. This means that when overall spatial input patterns remained the same, stimulus strength determined the type of surround modulation. In fact, many researchers agree that both surround suppression and surround facilitation are driven by these

lateral connections within V1 (e.g., Blakemore & Tobin, 1972; Carpenter & Blakemore, 1973; Nelson & Frost, 1985; Wenderoth, O'Connor & Johnson, 1986).

In one of the earliest studies addressing orientation surround effects, Blakemore, Carpenter and Georgeson (1970) interpreted psychophysical data in the context of the then newly discovered orientation selective cortical cells. Participants were asked to estimate the angle of two adjoining lines. Participants greatly overestimated 10 degree angles. Blakemore et al. (1970) explained these findings in terms of mutual inhibition of cortical columns. The population response of each line can be represented as a distribution with the peak at the orientation of the line and an inhibitory area around the peak. If you sum the population responses to each line you get a distribution of responses to both lines. The linear summation of this excitation and inhibition leads to two response peaks pushed slightly away from each other, which would cause the observed perceptual repulsion (see Figure 5 for a cartoon of response change to one of the lines). Carpenter and Blakemore (1973) propose the peak shift model to describe how responses to two lines can interact through horizontal connections to cause a shift in neural and perceptual responses.

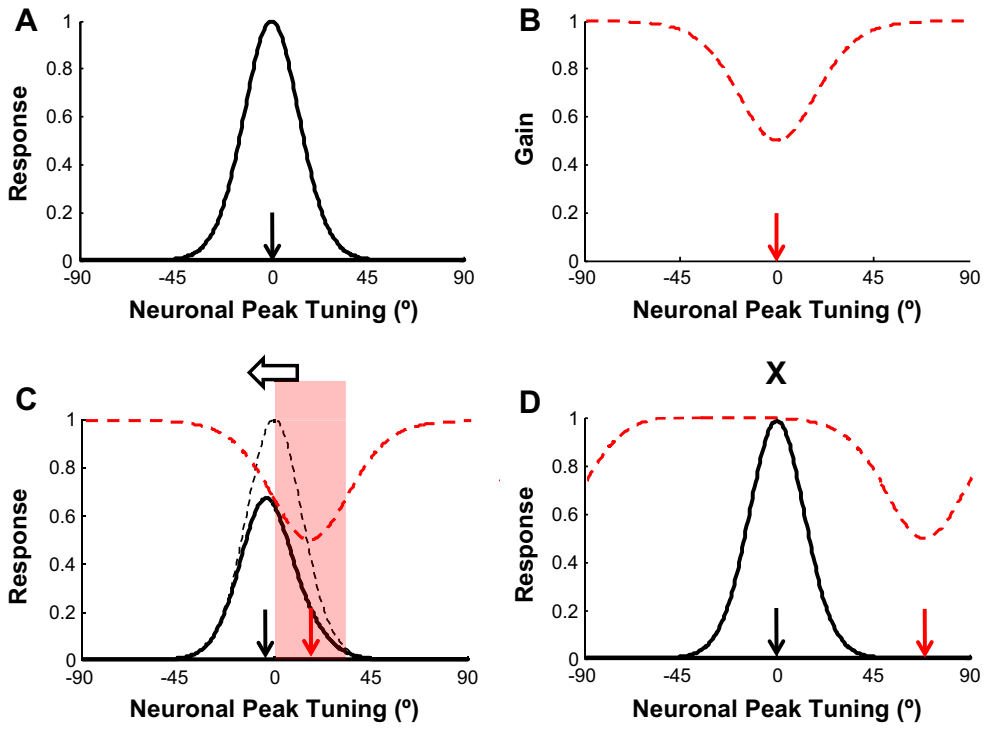

Figure 5. Cartoon of peak shift model of surround suppression, taken from Clifford (2014). (A) The response to a vertically oriented target stimulus is symmetrical and centered over the stimulus orientation. (B) The red dotted line represents the suppressive input from neurons tuned to a vertical orientation. (C) The addition of a suppressive input from neurons that respond maximally to 20 degrees will shift the peak response of the vertically oriented target stimulus. This shift is repulsive. (D) However, the original peak shift model cannot predict the faciliatory effects seen with 75 degree surrounds.

Although Carpenter and Blakemore's model provides an effective explanation of the perceptual repulsion seen with two lines with relatively small angular differences, it cannot account for the attractive perceptual effect seen with larger angular differences. O'Toole and Wenderoth (1977) extended the peak shift model by adding an area of disinhibition outside of the inhibitory area (an idea from Georgeson, 1976). When regions of disinhibition line up near the main peaks, they sum to create a small attractive effect (see Figure 6). This area can disinhibit by either being tuned to different orientations at the same location, or by being tuned

to the same orientation at different locations (see Figure 7; O'Toole and Wenderoth, 1977; Dragoi & Sur, 2000). For example, when cross-oriented stimuli inhibit each other it leads to disinhibition and a decrease in surround suppression (Cavanaugh et al., 2002). The disinhibition driven facilitation effect will always be smaller than the repulsive effect, which is driven by inhibition. This is because disinhibition can only reduce the inhibition that is already present. Disinhibition has been supported as a viable mechanism for surround facilitation (especially with collinear facilitation - Clifford, 2014; Gilbert and Wiesel, 1979; Stettler, Das, Bennett & Gilbert, 2002).

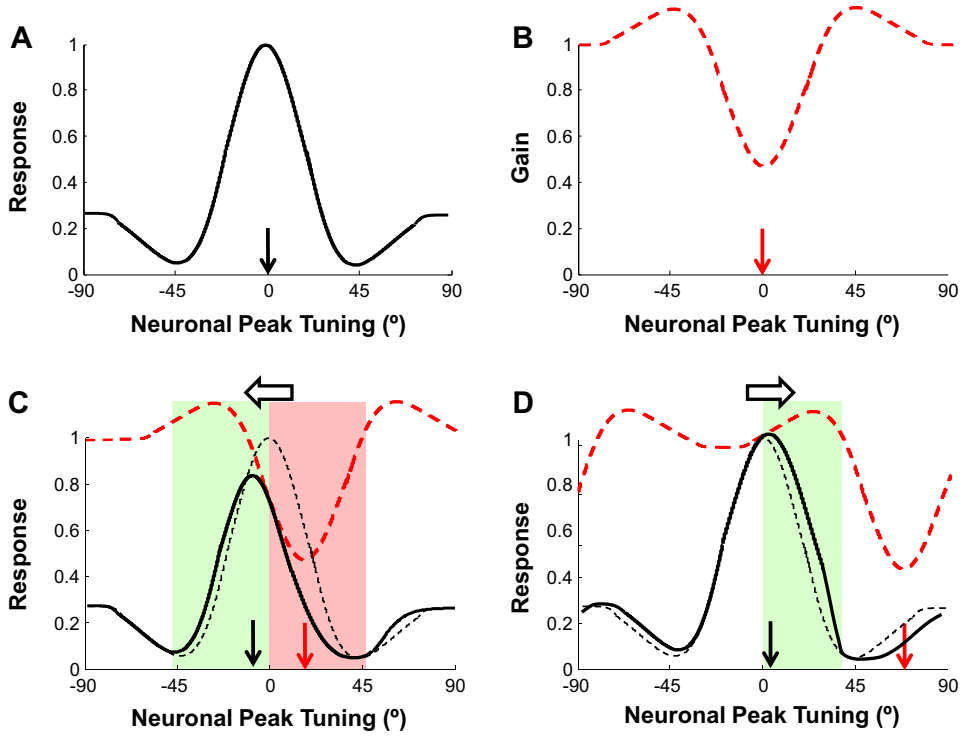

Figure 6. Cartoon of extended peak shift model of surround suppression and facilitation, taken from Clifford (2014). (A) The response to a vertically oriented target stimulus is symmetrical and centered over the stimulus orientation. (B) The red dotted line represents the suppressive input from neurons tuned to a vertical orientation. It also includes an area of disinhibition. (C) The addition of a suppressive input from neurons that respond maximally to 20 degrees will shift the peak response to the vertically oriented target stimulus. This shift is repulsive. (D) When the area of disinhibition lines up near the peak of the center response, the

peak of the center response will shift in the direction of the surround. This shift is attractive.

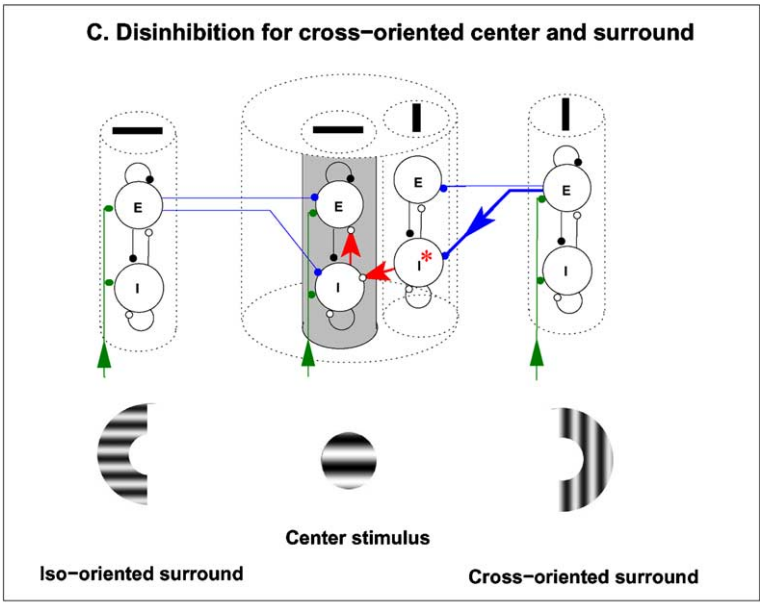

Figure 7. Cartoon of Dragoi and Sur's (2000) model of disinhibition, taken from Series et al. (2003). The green arrows represent feedforward activity, the blue arrows represent long range horizontal connectivity and the red arrows represent horizontal connections between neurons which respond to the same local area. Here, iso-oriented surrounds suppress center responses while orthogonally oriented surrounds facilitate center responses through disinhibition. Disinhibition occurs when orthogonally oriented surround neurons excite orthogonally oriented center neurons, which then inhibit the inhibitory response to the center.

While there is ample support for lateral connections driving surround effects, it is possible, and likely, that there is additional modulation coming from higher areas through feedback connections. Although Stettler et al. (2002) argue that the more dense lateral connections likely drive contour integration, they also demonstrate that both horizontal and feedback connections represent overlapping areas (also see Schwabe, Obermayer, Angelucci & Bressloff, 2006). Here, they compared the extent of these connections by linking connection maps to orientation tuning maps and found that both intrinsic horizontal connections and feedback from

V2 to V1 cover approximately 7mm of cortical distance (4 degrees visual angle in retinotopic distance). However, feedback connections from other higher areas can integrate information over a larger retinotopic distance (Angelucci & Bullier, 2003).

Horizontal connections alone are too slow and sparse to account for all of the surround suppression seen in V1 (Angelucci & Bullier, 2003). Feedback connections tend to be fast and cover a large area (Angelucci & Bullier, 2003) but are not orientation specific (Stettler et al., 2002). Feedback connections may be responsible for the modulatory effects of surround regions that go beyond the distance of horizontal connections (see Figure 8). Angelucci and Bullier (2003) propose that horizontal connections cover the CRF and the near surround, which can experimentally be defined as the area of low contrast summation. Feedback connections likely cover the other areas where surround suppression occurs but is too far for horizontal connections to reach. There is also evidence that cooling or pharmaceutically decreasing the activity of the higher visual areas leads to less surround suppression from far regions (Hupé et al., 1998). Kim and Freeman (2014) state that surround effects are likely initially driven by fast feedback connections and then slower orientation tuned horizontal connections.

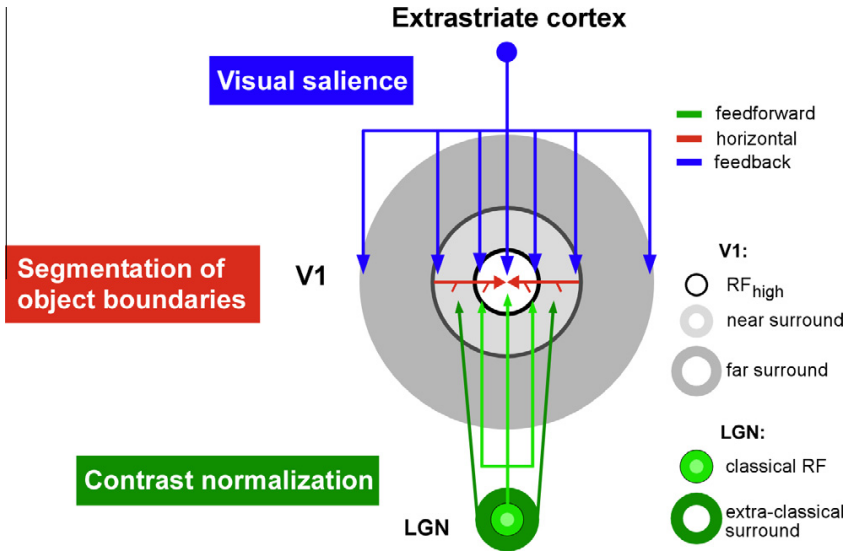

Figure 8. Angelucci and Bullier's (2003) figure depicting the extent of coverage of feedforward, feedback and horizontal connections to the CRF. Here, they specifically defined the CRF as the RF for a high contrast stimulus. The RF for a low contrast stimulus is defined as the near surround.

However, Wenderoth and Johnstone (1988; also see Poom, 2000) suggest that these connections actually drive separate effects. They propose that the attractive and repulsive effects are probably caused by different mechanisms. They note that the repulsive effects are reduced by situations that reduce lateral inhibition (i.e., gap or distance), while the attractive effects are reduced by situations that provide global orientation cues, such as the addition of a frame. This type of method will be discussed further in the Timing and Segmentation section. These results imply that lateral connections drive the surround suppression effect while feedback connections drive the surround facilitation effect. This seems like an extreme case. A more likely scenario is that horizontal connections are involved in facilitative effects and they can also be modulated by feedback.

In summary, perceptual repulsion and attraction are predicted by the linear summation of population responses coming from lateral inhibition and disinhibition. However, lateral connections alone cannot account for the extent of all surround effects. Lateral connections are limited by the distance they can span and the speed at which they can propagate information. Feedback connections can send information from a larger area very quickly but are not orientation specific. It is likely that the perceptual surround effects are from a combination of fast feedback connections and slower orientation specific lateral connections.

Modeling spatial integration

Throughout the years there have been several theories to explain the neural and perceptual tilt effects of surround stimuli.

One of the earliest theories was the Normalization theory by Gibson and Radner (1937). The main idea behind this theory is that the horizontal and vertical orientations are considered the "norms" of visual orientation. When a large area of the visual field is tilted, the nearest norm will shift toward the new orientation (i.e., the vertical reference is shifted). This causes the test stimulus to appear to be shifted in the opposite direction. This model can account for both the repulsive and facilitative perceptual effects. For angles 1-45 you can think of the repulsive TAE as being opposite of the tilt to the right of vertical. For angles 45-90 the TAE is attractive but you can think of it as repulsive if you consider it is opposite the leftward tilt from *horizontal*. However, this model does not account for the asymmetry of effect magnitudes.

Recently, more precise models have been developed to describe the neural computations involved in spatial integration (for review see Schwartz, Hsu & Dayan, 2007). There are several neural responses that can be modeled. Populations of neurons in the CRF that are tuned to the same orientation as the contextual stimulus (iso-oriented surrounds) will undergo a suppressive effect. This suppressive effect can be modeled in several ways including: a reduction in firing rate, a relative increase in tuning width, and a shift (away from the context orientation) in tuning preference. There are also several psychophysical responses to surround stimuli to model including the repulsive effect, the attractive effect, and changes in discrimination thresholds (sensitivity). These psychophysical effects can be decoded from the neural responses using maximum likelihood methods. Below I will describe structural, phenomenological and optimized models for predicting neural and/or perceptual effects of surround integration.

Structural models

Structural models describe the biophysical aspect of neural mechanisms and often rely on physiological data. These models can be interesting because they must account for the dynamic and flexible effects of contextual surrounds using what is known about the neural connections. Below I will provide modeling evidence to support the proposed neural connections involved with spatial integration.

One of the key findings in the neural literature is that the contrast or strength of the stimulus determines the direction of the surround effect. Stemmler et al. (1995) model the circuitry of connections in hypercolumns, which determines the relative amount of excitation and inhibition reaching the target cell. Here, they

model each hypercolumn as a collection of inhibitory and excitatory cells. The circuits between the cells determine the balance of excitation and inhibition of surround responses (See Figure 4). The model describes an asymmetric effect of inhibition and excitation. That is, inhibitory neurons have a higher threshold as a way to cap excitation. They do not respond to weak visual input but they do respond to strong visual input. This leads to a small amount of facilitation for a weak excitatory surround. This modeling of the responses can explain why some researchers find an increase in the RF size for low contrast stimuli – a low contrast surround beyond the CRF would yield a small amount of facilitation from excitatory lateral connections, which would cause the response to look like a larger RF. They also add long-range horizontal connections between excitatory and inhibitory neurons that have similar orientation preferences. This would lead to orientation specific surround effects that change the balance of excitation and inhibition.

In addition to the contrast of the stimulus, the relative orientation of the surround influences the overall direction of the surround effect. Cross orientation surrounds cause facilitative responses but iso-oriented surrounds lead to suppressive responses (Levitt and Lund, 1997). Dragoi and Sur (2000) model the neural circuits and determine that cross orientation facilitation is from disinhbition (see Figure 7). Local inhibitory cells within the CRF are broadly tuned to orientation and therefore respond to orientations outside the central cells preferred orientation. Long-range excitatory connections are much more orientation specific and connect with cells that have similar orientation tuning preference. According to their model, iso-oriented surround suppression happens when there is the

excitation of a local inhibitory neuron with the same orientation preference as the central cell. Cross-oriented surround facilitation happens when local inhibitory neurons are disinhibited by inhibitory neurons that have the same orientation preference of the surround. This theory is contentious because others have reported that there are no inhibitory connections between orthogonal orientations (Ferster and Miller, 2000), but it is possible that this disinhibition happens at the pinwheel locations of the cortex (Das & Gilbert, 1999).

As we saw above, much of surround suppression is thought to be from lateral connections but it doesn't seem possible that lateral connections would be able to account for influences from distant surrounds. Lateral connections are not long enough or quick enough to produce all observed perceptual effects (Sceniak et al., 2001; Cavanaugh et al., 2002; Levitt & Lund, 2002). Feedback connections can cover more area (Angelucci & Bullier, 2003) but only send excitatory signals to excitatory neurons (Johnson & Burkhalter, 1996; Shao & Burkhalter, 1996) so they were previously not considered for the circuitry of surround suppression. However, Schwabe et al. (2006) describe an anatomically and physiologically constrained recurrent network model that depicts how feedback connections could drive far surround suppression (see Figure 9). In this model, feedback connections stimulate horizontal connections that connect with excitatory or inhibitory cells in the CRF. The local lateral inhibitory neurons have a higher response gain and contrast threshold than the central cell so weak stimulation will not activate these inhibitory connections but it will activate excitatory connections. Therefore, surround effects

will be facilitative at low stimulation levels and suppressive at higher stimulation levels.

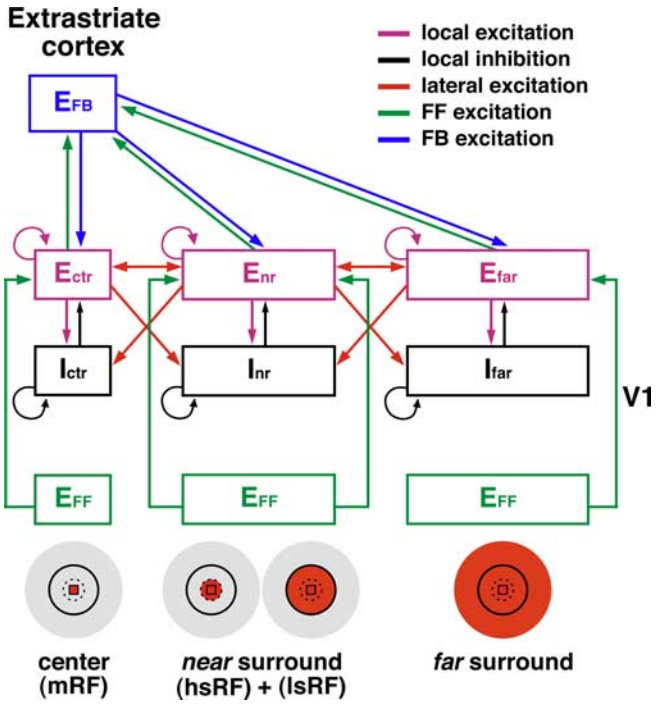

Figure 9. Recurrent network model, taken from Schwabe et al. (2006). This model demonstrates how excitatory feedback connections can trigger horizontal connections to give rise to far surround suppression and surround facilitation.

In summary, structural models can predict neural and perceptual effects by modeling the circuitry of the visual system. Lateral connections can excite or inhibit local central responses to a target. These lateral connections may be activated by feedforward, horizontal or feedback connections. The asymmetric effect of suppression/facilitation occurs when local inhibitory neurons have a higher activation threshold than local excitatory neurons. This predicts facilitation with weak stimulation. Cross-oriented facilitation can also occur through lateral disinhibition. These models use biologically plausible circuits to predict these effects.

Phenomenological models

Phenomenological models, also known as functional models, describe processes within the context of the visual system. These processes may occur elsewhere in the brain as well. By examining these processes in the context of the visual system we can begin to understand the computations that arise from the neural circuitry.

An extended receptive field (ERF) can be thought of as a single entity that is a combination of the CRF and eCRF (Sceniak, Ringach, Hawken & Shapley, 1999). This entity can be described by a difference of Gaussian (DoG) model (see Figure 10). Here, there are two overlapping mechanisms that are interacting subtractively, 1) an excitatory CRF, and 2) a suppressive surround. Both of these mechanisms are represented by their own Gaussians and are centered over the same position. The response then is the difference between the center gain multiplied by the center Gaussian, which is proportional to the radius of the grating stimulus, and the surround gain multiplied by the surround Gaussian, which is also proportional to the radius of the grating stimulus.

An alternative model was proposed by Cavanaugh et al. (2002), which uses a divisive mechanism rather than a subtractive one. They refer to this as the Ratio of Gaussians (RoG; see Figure 10). While a subtractive mechanism would simply shift the response curve down, a divisive mechanism scales the response curve. This type of response change is consistent with nonlinearities seen in neural responses (Albright & Stoner, 2002). The RoG model is similar to a normalization model, which also relies on a divisive mechanism and will be discussed below.

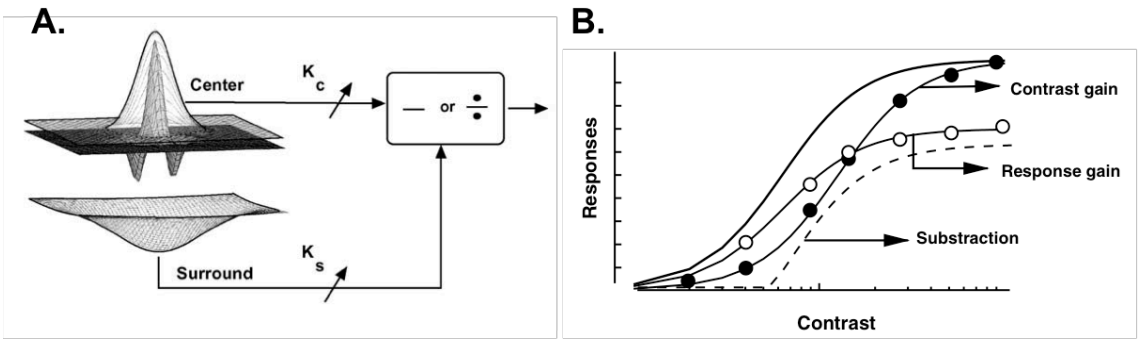

Figure 10. The DoG and RoG models describe the interaction between response distributions to the center and surround stimuli. A) Here, the center response is represented as a Gaussian envelope around a gabor stimulus. This Gaussian is either linearly suppressed by the surround Gaussian (DoG) or divisively suppressed (RoG). B) Examples of types of suppression for contrast responses. The DoG model would predict subtraction, which reduces the response at all contrasts equally. A model of divisive normalization would predict a response gain or a contrast gain change. A response gain change will scale the responses at all contrasts by a ratio. The response gain is what is predicted by the RoG model and is the best description of surround suppression.
A contrast gain change will scale the responses without affecting the maximum response. This type of response can describe within CRF normalization. This figure was constructed by combining two figures taken from Series et al. (2003).

Divisive normalization and gain control

The neural computation of spatial integration can be described by a type of divisive normalization. Normalization can be thought of as a standard computation that occurs across brain regions and processes. Normalization occurs when a neural response is divided by a common factor that is the summed activity of a pool of neural responses (Carandini & Heeger, 2012). Divisive normalization can help to reduce redundancies in perceptual processing (and general neural representation). Heeger's (1992) standard gain model uses a single neuron in V1 but this model can also be applied to other types of neurons and even population responses (Carandini & Heeger, 2012). Here, the response of a target neuron's CRF (R_c) is a function of the feedforward (f_c) activation divided by the gain control signal (Υ_{gain}).

$R_c = f_c / \Upsilon_{gain}$

The feedfoward activation is determined by the RF filtering of the stimulus (this involves convolving the stimulus with the tuning function). The gain control signal is the squared feedforward response of other activation from the center and surround locations, not included in the feedforward activation of the CRF of the target neuron.

The filter activations of the gain (f_c and f_s for the center and surround areas) convolve the part of the image is associated with tuning functions of the center and surround. If the image is a natural scene then there will be joint statistics between the areas activating each neuron. Therefore, the center and surround responses will be correlated. This correlation shows areas that have redundant information and these areas of redundancy are put into the gain pool. The gain pool then removes this redundant information by divisively normalizing the neural response.

A Gaussian Scale Mixture model (GSM) can capture the statistical coordination between the center and surround as a way to set the gain pool (Schwartz et al., 2009). Here, the statistically coordinated components of the center (l_c) and surround (l_s) responses are determined by a mixer (v). The GSM is related to divisive normalization because you can divide out the mixer to get the local Gaussian form (g). The authors are able to estimate the local center form (g_c) given the modeled activation of the center and surround.

$l_c = vg_c \qquad l_s = vg_s$

Like the standard gain model described above, here the gain is set by taking the square of the sum of squares of the surround activations (plus a constant to keep it above 0). You can include many surround units in the gain pool. The activation of the surround only affects the local (i.e., center) Gaussian form if they are in the same gain pool (see Figure 11). The center and surround will only be in the same gain pool if they are statistically coordinated. With orientation selectivity, that means that for a surround to affect the central response it must respond to a similar orientation at a different spatial location. When center and surround are not part of the same object, the surround activations are not included in the gain pool. In the full flexible model of normalization, these two cases of center and surround co-assignment can be combined and weighted by the probability of each case. That is, the normalization effect of the surround will be weighted by the probability that the center and surround are part of the same object. Therefore the cortical output of the model is a Bayesian estimate of the local distributions given the dependencies between them.

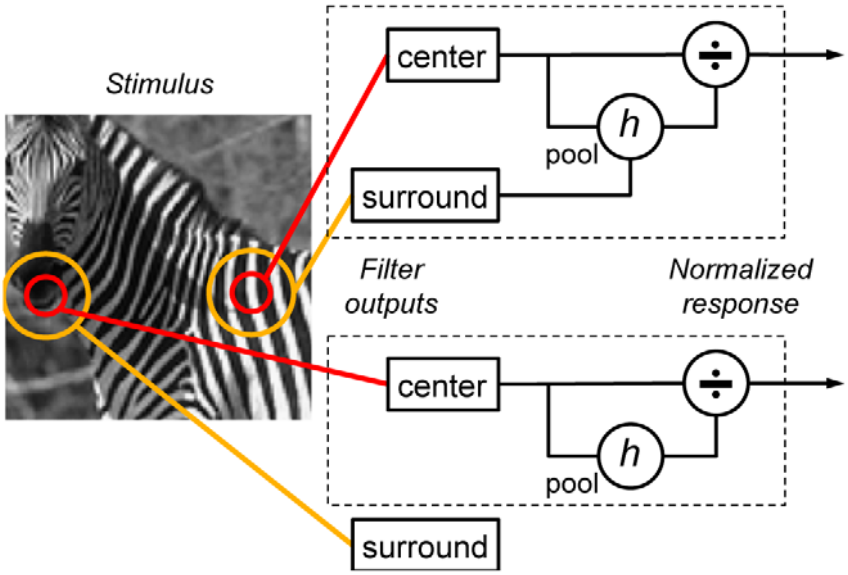

Figure 11. Flexible normalization of the center response. When the center and surround are part of the same object they will be statistically coordinated and the surround activation will be included in the normalization pool. When the center and surround are not part of the same object the surround will not be included in the normalization pool. Figure taken from Coen-Cagli, Dayan & Schwartz (2012).

We can extend these models to populations of neurons by describing them as a distribution of center orientation preferences (Schwartz et al., 2009; Reynolds & Heeger, 2009, see Figure 12). Neurons with high activations have orientation tuning preferences near the stimulus orientation, leading to the distribution peak being centered over the stimulus orientation. Each central unit has surround units with the same orientation preference in its gain pool. The amount of normalization from the surround units to the center units will depend on the probability of the center and surround being co-assigned and the amount of activation of each. When the surround is about 15 degree different from the center, it will skew the distribution of the center in a non-linear way due to the effects of the normalization. This leads to a repulsive perceptual shift.

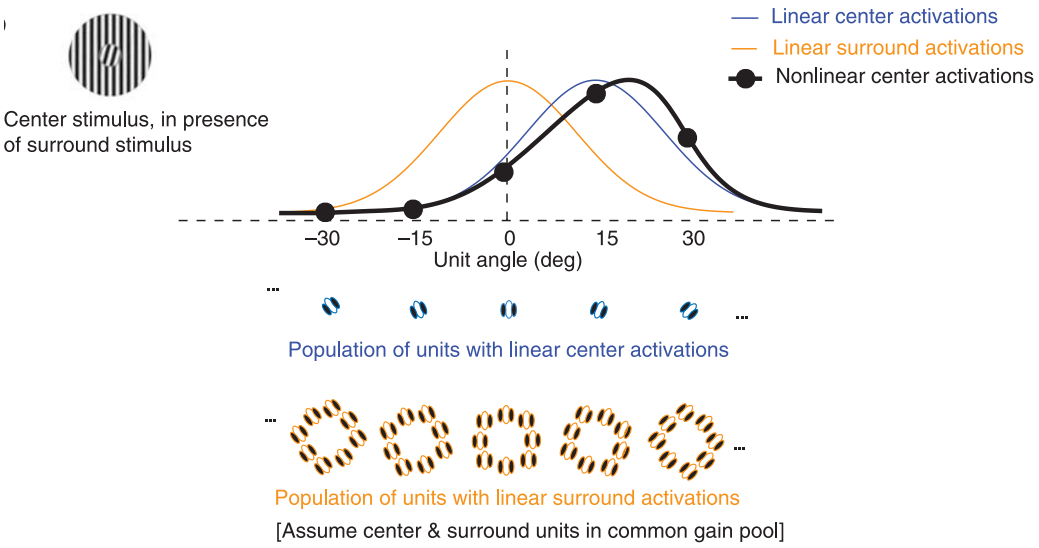

Figure 12. Cartoon of the population responses of center and surround stimuli. Alone, the center activation is symmetrically distributed around the orientation of the center stimulus. This activation is nonlinearly affected by the gain normalization from surround units that share the same orientation preference. Here, a 15 degree difference between center and surround orientations leads to a perceptual repulsion. Figure taken from Schwartz, Sejnowski, & Dayan (2009).

Perceptual enhancement can occur when the preferred center orientation is far from the surround orientation. This is because the surround activity will only weakly activate surround units with the same orientation preference as the center. This gives the peak center response only a small normalization pool. When the normalization pool activity is small and the central activity is large it provides evidence to the system that the common mixer is small. Therefore, the system will estimate the local Gaussian as being large. However, if the weak activation is not predicted to be in the same gain pool then it will not have an enhancing effect because it will not provide evidence about a common mixer. In the case when this enhancement occurs, it can lead to a perceptual attractive effect.

In summary, normalization is a standard computation in the brain, which can be applied to spatial integration. Areas of the visual field are normalized with divisive gain control to remove statistical redundancies. Surround suppression can be thought of as a form of normalization by which similarly oriented areas are pooled together and the response is divided by a common factor of the pool. Surround facilitation can occur when the center and surround are somewhat statistically coordinated but the surround only weakly activates the central neurons (i.e., when the center and surround have very different orientations). The predictions of divisive normalization are consistent with the neural and perceptual surround effects.

Optimized models

Optimized models predict neural data from an optimized strategy of visual encoding. Based on information theory, neural responses have adapted to remove redundancies (Attneave, 1954). Schwartz and Simoncelli (2001) demonstrate that a variant of an RoG model with divisive normalization will reduce the redundancies of the long range correlations within natural images.

Efficient neural networks learn the statistical regularities of the natural world and only represent deviations from what is predicted (Atick, 1992). Rao and Ballard (1999) developed a model where each visual level tries to predict the responses of the lower level. For example, V2 would try to predict the response of V1 using feedback connections. The error, or difference between the actual response and the predicted response is sent as a feedforward message up to the next level. When they model what the RFs would look like they get simple cell-like RFs and end

stop RFs. This suggests that long edges are more common in nature than short edges: when edges are long the cell stops responding because that is what would be predicted. In this sense, center and surround interactions can be modeled as the response from the detection of residual errors, based on what would be predicted for a natural scene.

Prior experience with natural scenes would then impact the perception of a stimulus in the context of other stimuli. Schwartz et al. (2006) propose that we have a smoothness prior. That is, we expect most line segments shared by an object to be smoothly connected. Using a Bayesian framework, the authors were able to predict orientation bias of a central line in the presence of flankers (see Figure 13). The prior can be thought of as a Gaussian centered over the optimal orientation with the addition of a baseline that predicts the likelihood of this smoothness configuration. This is multiplied by a Gaussian that is centered over the actual orientation of the target line to give the posterior distribution. By computing probability of each central angle, given the flanking angles, you can produce a psychometric function and extract the "perceived" target angle. The bias of a central line in the presence of flankers will go in the direction that will favor a smooth configuration. The results from this modeling are consistent with the psychophysical results from Kapedia et al. (2000), which will be discussed further in the Surround Regions section. These results suggest that our misjudgments of orientation could actually be optimal inferences about the relationship between regions of a stimulus or scene.

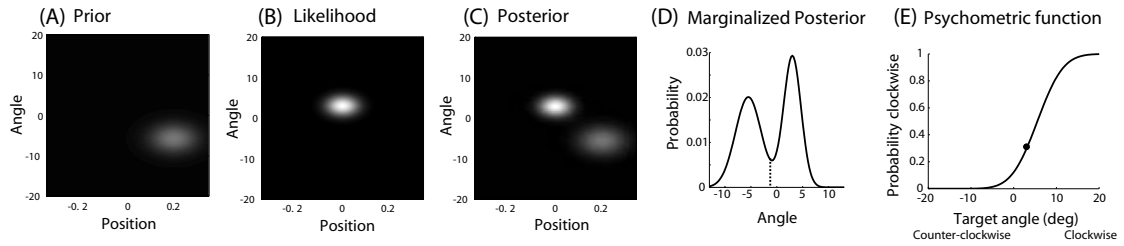

Figure 13. A) Prior distribution is represented as a Gaussian centered over the orientation and position of the central line with the smoothest configuration for a given context. B) The likelihood distribution is the Gaussian centered over the orientation and position of the actual central line. C) The prior and likelihood are combined to give the posterior distribution. D) The marginalized posterior is the 1D distribution of the posterior collapsed over position. Here the dotted line shows the mean. E) By calculating the probability that the mean is clockwise you produce a single point on the psychometric function. This figure was taken from Schwartz, Sejnowski and Dayan (2006).

In summary, models of neural circuits help us to understand the underlying neural structures involved with spatial integration. These circuits compute normalization processes, which lead to neural and perceptual surround effects. Divisive normalization, acting through lateral inhibitory circuits, reduces redundancies of scene statistics and makes neural processing more efficient. This efficiency also leads to illusory effects depending on how the normalization pool is formed. Determining which areas are pooled will depend on the statistical regularities of the scene and prior experience with these regularities. Neurons upstream may predict how this pooling will occur and signal this through feedback connections. Errors in predictions may manifest as center surround interactions.

Timing and Segmentation

Now that I have described some of the basic theories and the proposed circuitries behind the neural and perceptual surround effects, I will introduce some of the ways researchers use perceptual data to make inferences about underlying

neural connections. Two ways that perceptual researchers can test types of neural connections is by altering the timing and segmentation of their stimuli. By making assumptions about the limits of the lateral neural connections, researchers are able to attribute perceptual effects to different types of configurations (e.g., horizontal, feedback, and feedforward).

There are two main ways that contextual flankers could modulate response to a test stimulus. One way is through horizontal interaction connections (i.e., lateral inhibition). These horizontal interactions are relatively slow because they have unmyelinated connections. The other is through feedback from extra-striate areas. This feedback is predicted to be quicker than horizontal connections because the information is carried on myelinated axons (Angelucci & Bullier, 2003). If the contextual modulation were driven by lateral connections, then we would expect that the time for the modulation (i.e., minimum time for significant difference between baseline and context conditions) would increase with distance between center and surround. This is because the time it will take for the signal to propagate through unmyelinated axons will increase with distance. If the contextual modulation were driven from feedback from extra-striate areas, then we would expect that the time for modulation would be consistently quick regardless of surround distance.

To test these predictions, Cass and Spehar (2005a) presented participants with target Gabor patches surrounded by two flanking Gabor patches using the spatial and timing predictions described in the paragraph above. The participants were asked to detect changes in contrast from the test patch. The flankers were

either positioned collinearly or laterally. Based on how the effects manifested in time, the authors found that collinear iso-oriented contrast facilitation was likely driven by horizontal connections but that lateral iso-oriented contrast facilitation was likely driven by feedback connections. This is also supported by Cass and Spehar (2005b).

Using a full surround, Bair, Cavanaugh and Movshon (2003) show that iso-orientated neural surround suppression has a small delay with distance for many neurons, but that this delay was still too quick to be from a horizontal connection in half the cells recorded. They determined that surround suppression is likely from feedback connections from extrastriate areas that project to local inhibitory neurons. Because they were using a full surround it is possible that they measured the combined effects of horizontal and feedback connections that Cass and Spehar (2005) showed regionally. The combined effects could appear to be just feedback effects because they would be brought about more quickly than the horizontal effects.

Another way that we can get information about the types of connections that are driving perceptual effects is by introducing a gap between the surround and target stimuli. Horizontal connections are limited by the distance that they can span in the cortex (about 8mm, Gilbert & Wiesel, 1989). In fact, the repulsive perceptual effect is reduced by adding a gap between the center and surround stimulus (Tolhurst & Thompson, 1975). In contrast, the attractive effect remains unaffected (Wenderoth & Johnstone, 1988) by the presence of the gap. Furthermore, Smith and Wenderoth (1999) found that they could manipulate repulsive effects of the STI

with contrast and spatial frequency, but that these attributes did not affect the attractive effects. They came to the conclusion that the two effects likely are processed by different mechanisms: the repulsive effects from lateral connections and attractive effects from feedback connections.

Alternatively, Kim and Freeman (2014) show that both surround suppression and facilitation rely on both feedback and horizontal inputs. One reason others may have found differences between how the effects are modulated by a gap could actually be that the area of the stimuli varied with gap size (i.e., a larger gap led to a smaller surround annulus, since the outer diameter of the annulus was fixed). The authors demonstrate that suppressive effects require higher levels of stimulation and are reduced with a reduction in annulus size. When the surface area of stimulation is held constant the suppressive effects remain constant. Facilitative effects occur with weak stimulation and are not affected by annulus size or surround distance. Although both feedback and horizontal connections are involved in these processes, the authors propose that the orientation specific effects arise from slower horizontal connections. This is evidence that suppression and facilitation are driven by the same mechanisms.

Additional studies on timing and segmentation have also suggested that both the attractive and repulsive effects are driven by the same mechanism. Mareschal and Clifford (2012) determined that the timing effect of an unconsciously perceived surround influences the attractive and repulsive effects in similar ways. They presented participants with a dynamic version of the STI where the orientation of the surround changed throughout the presentation of the center. Using reverse

correlation the authors were able to extract the effects of surround orientation on perception of the orientation of the center at different timepoints. They found that both the attractive and repulsive effects had similar onset times.

This was also true when there was a small gap between the center and surround, with both the attractive and repulsive effects decreasing with this gap. These results suggest that both the attractive and repulsive effects of the STI are driven by the same mechanism. Also, Kapedia et al. (2000) found that both attractive collinear and repulsive lateral flanker (orientation) effects decreased when flankers and target were separated by more than 8 minutes of arc. Given that lateral connections are limited in their physical reach, it is likely that both of these effects are processed through lateral connections. Mitzobe et al. (2001) found that both neural contrast facilitation and contrast suppression effects occur for flankers that are up to 12 degrees apart. While this suggests a common mechanism, it may be better explained by multisynaptic lateral connections or feedback, which cover more area. On the other hand, Polat and Sagi (1993, 1994) found that up to two wavelengths away (.3 degrees) from the center stimulus was a suppressive region of flanker contrast modulation, but that between two and ten (3 degrees) wavelengths away there was a facilitative region. It is possible that these differences are still due to the same lateral mechanism but that the strength of connections decreases with distance, leading to a facilitation effect. Therefore, although researchers occasionally find differences in how distance modulates the facilitative and suppressive effects, it is still possible that these effects are both driven by a combination of lateral feedback connections.

Aside from pressing the physical limits of the neural connections, there is also evidence that *perceptual* segmentation will reduce the tilt effects. Van Der Smagt et al. (2005) showed that surround suppression was partially relieved in V1 neurons when there was at least one segmentation cue, in this case relative orientation or contrast polarity, but combining the cues did not reduce the suppressive effect any further. This partial recovery from neural surround suppression led to a full recovery from the perceptual repulsive effect. Furthermore, Qiu et al. (2013) show that contrast, disparity and geometric arrangement act as perceptual segmentation cues that reduce the repulsive perceptual effect. Combining these cues does not reduce the effect further. Likewise, Durant and Clifford (2006) determined that the maximum contrast effect is reduced by perceptual segmentation cues (i.e., gap or asynchronous presentation between center and surround) but is not reduced further by combining segmentation cues. This reduction in neural and perceptual surround integration may be connected to how perceptual segmentation cues impact gain control.

Modeling research by Schwartz et al. (2009) suggests that center surround interactions are affected by how the components are perceptually grouped. Their model treats the relative difference between features of center and surrounds as a cue to determine if they cross a segmentation boundary. Areas that do not appear to cross segmentation boundaries are assigned to the same gain pool. Surrounds that are across segmentation boundaries have less of an influence on response to the central stimulus. It seems that adding additional segmentation cues does not further reduce the illusory effects. Therefore, it seems like the presence of a single

segmentation cue is enough to reduce the probability of co-assignment of the surround to the center's gain pool.

In conclusion, most researchers agree that the repulsive perceptual effect is driven by lateral inhibitory connections within V1 (Kapedia et al., 2000; Kim & Freeman, 2014; Mareschal & Clifford, 2012; Smith and Wenderoth, 1999; Tolhurst & Thompson, 1975; Van Der Smagt et al., 2005; but see Bair et al., 2003 for surround suppression from feedback). Some research has provided evidence that the attractive effect is driven by feedback connections (Wenderoth & Johnstone, 1988; Smith and Wenderoth, 1999). However, the conditions in these studies may be confounded by the fact that the stimuli differentially affect the suppressive and facilitative effects. Many researchers conclude that the attractive effects are also from lateral connections (Kapedia et al., 2000; Kim & Freeman, 2014; Mareschal and Clifford, 2012). It is also possible that both effects are driven by lateral connections as well as feedback connections. There is also some evidence that the relative contribution of different connections depends on the spatial arrangement of the surround stimuli (Cass & Spehar, 2005).

To summarize the Timing and Segmentation section, researchers are able to use perceptual paradigms to learn about the underlying neural mechanisms of perceptual effects. By manipulating the timing and positioning of surround stimuli we are able to test assumptions about neural connections between the center and surround. Physically or perceptually segmenting stimuli reduces the perceptual surround effects. This may be because it surpasses the limits of the neural structures that are driving the effects. It is important to control the area of the

stimulus when adding a gap to avoid confounding distance with level of stimulation, which may affect attractive and repulsive effects differently. It also may be that the cognitive mechanisms (i.e., segmentation and gain control) that calculate the perceptual effects use these cues to determine how to pool the surrounding information. As we will see next, the physical location is also an important modulator of perceptual effects that can inform us of underlying neural mechanisms.

Surround regions

Not all areas of the surrounding stimulus lead to the same neural or perceptual effects. Depending on the position of the inducing stimulus the effect may be attractive/facilitative or repulsive/suppressive. These different spatial effects may help us to group and segment surfaces. Collinear facilitation may help to increase the saliency of lines that are connected, while lateral suppression may inhibit areas where the same orientations are present (Field, Hayes & Hess, 1993; Kapedia et al., 2000; Knierim & Van Essen, 1992). In fact, there seem to be some neurons that asymmetrically respond to collinear stimuli (end inhibited; Hubel & Weisel, 1965), or lateral stimuli (side inhibited; Bishop, Coombs & Henry, 1973).

Kapedia et al. (2000) explored the spatial distribution of contextual interactions in V1 by looking at the spatial arrangement of interactions for responses in V1 and perception. They mapped out the receptive field surround (both physiologically with monkeys and psychophysically with humans) to identify areas where there are inputs underlying excitatory modulations and inputs for inhibitory modulations. To map out this area physiologically, two monkeys were

briefly presented with bars in their periphery. The optimal receptive field area and orientation preference for specific cells was determined. This receptive field area was used as the CRF. The neural response was then recorded from each cell with stimuli presented alone (in the CRF) or with flankers (in regions of the eCRF). To map out the areas for the perceptual effects, participants were presented with a test line stimulus with or without flankers. Using psychophysical and neural data, the authors found that excitatory regions tended to be collinear to the test line, while inhibitory regions tended to be lateral to the line. Perceptual effects paralleled these findings, with small angular differences in collinear flankers leading to an attractive effect while lateral flankers lead to a repulsive effect. However, the difference in orientation between the flanker and target changes the magnitude of this effect, with both becoming repulsive at larger angles (see Figure 14).

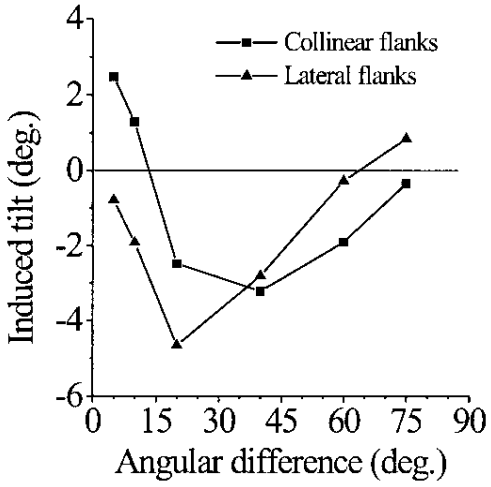

Figure 14. Perceptual tilt illusion magnitude for collinear and lateral flankers of different orientations. Positive numbers indicate an attractive effect while negative numbers indicate a repulsive effect. At small angular differences, collinear flankers lead to an attractive effect while lateral flankers lead to a repulsive effect. Figure taken from Kapedia et al. (2000).

Mizobe et al. (2001) also found that the collinear region was a source for excitatory neural input. Here, they studied contextual modulation using three gratings: two flankers and a central patch that was matched to CRF size, orientation and spatial frequency. They found that while facilitation and suppression could happen in the same cell, the collinear area was dominated by facilitative input. When the collinear stimuli were presented orthogonally to the central stimulus there was a reduction in facilitative input but not a reduction in the already minimal suppressive input. They developed a model of what the geometric relationship of the surround effects would look like (see Figure 15). Here, facilitation is inline with the collinear axis.

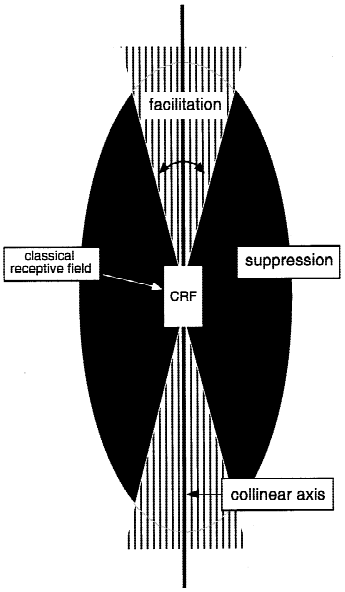

Figure 15. Mitzobe et al.'s (2001) cortical model of perceptual grouping based on the areas around the CRF that are facilitative and suppressive.

These regional effects are dependent on the relative contrast of the stimuli. Chen and Tyler (2008) mapped the area of the extra CRF as it relates to contrast facilitation. They determined that the eCRF surround regions are contrast

dependent. At low contrasts, the eCRF has facilitative regions collinear to the target, consistent with previous literature. However, at high contrasts, these same regions become suppressive (see Figure 16). This is consistent with the contrast dependent effects described above (e.g., Cavanaugh et al., 2002; Kapadia, Westheimer, & Gilbert 1999). In a more general sense, this could mean that when there is a small amount of surround stimulation the collinear region has a facilitative effect but when that stimulation passes a threshold the effect becomes inhibitory. As we have seen above, it seems that inhibition kicks in once stimulation reaches a higher threshold.

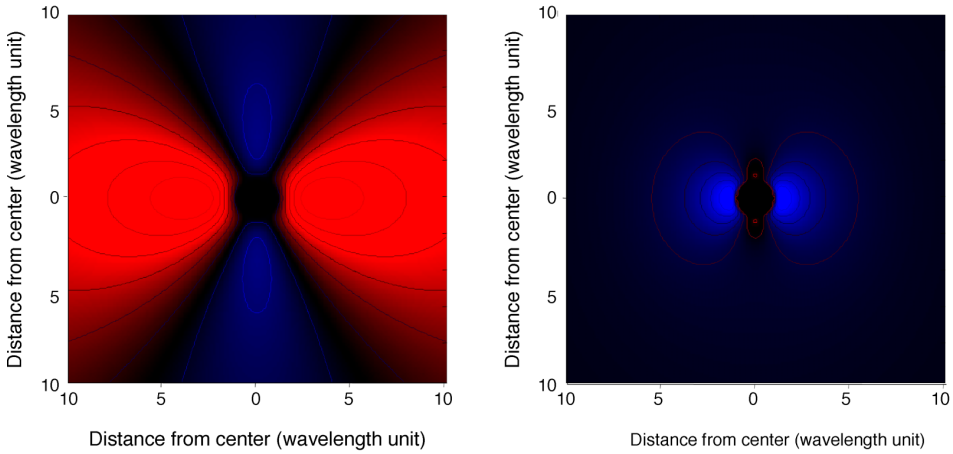

Figure 16. Estimate of eCRF. Red indicates excitatory regions and blue indicates inhibitory regions. The collinear axis of the RF is in line with the horizontal axis of the plot. Left: Target is presented at 5% contrast and shows collinear excitatory regions. Right: Target is presented at 50% contrast and shows collinear inhibitory regions. Figure taken from Chen and Tyler (2008).

If we interpret the contrast dependent effects more generally as strength of stimulation we may be able to account for some discrepancies in the literature. Like Kapedia et al. (2000) and Mizobe et al. (2001), Qiu et al. (2013) tested the modulatory effects of different surround regions on the perception of a central target. Qiu et al. (2013) presented participants with a central gabor and two flanking

gabors, rotated by 20 degrees. All flanking positions lead to a repulsive perceptual effect. The authors found that there was a slightly larger repulsive effect when the flanking gabors were positioned collinearly, than when they were positioned laterally. Although we typically think of the collinear positions as being a facilitative region, we must always consider the specific parameters of the stimuli. Here, the 20 degree tilt caused a small repulsive effect at the colinear positions. This is also true for Kapedia et al. (2000). The difference between these two studies is that Kapedia et al.'s (2000) data show a slightly larger repulsive effect for 20 degree lateral flankers compared to collinear, but Qiu et al. (2013) found a slightly larger repulsive effect for the collinear flankers compared to the lateral. It is possible that increasing the strength of the stimuli (i.e., going from Kapedia's simple flankers to Qiu's flanking Gabors) differentially affects the magnitude of the collinear and lateral influence. Therefore, increasing the stimulus strength in the colinear region would lead to a larger suppressive effect and a reduction of the lateral suppressive effect. This seems plausible given that the colinear position is more likely to be part of the same gain pool and therefore would have a stronger influence on the surround (Schwartz et al., 2006), which would increase with stimulus strength.

If we apply the Bayesian smoothing prior described by Schwartz et al. (2006) we can predict the perceptual tilt effects for lateral and collinear flankers of different orientations. For example, a small relative orientation difference for collinear flankers leads to a high probability of smoothness and a moderate attractive effect. However, to optimize smoothness between slightly tilted lateral flankers and a central vertical line, the central line would be tilted in the opposite

direction of the flankers. This is consistent with the results from Kapedia et al. (2000).

Giving the collinear surround position a higher prior probability of co-assignment with the center means that the collinear surrounds will modulate the center responses more than the lateral surrounds (Coen-Cagli et al., 2012). This modulation is dependent on stimulus strength. Coen-Cagli et al. (2012) model these effects and show that weak iso-oriented collinear surrounds drive a facilitative effect while strong iso-oriented collinear surrounds drive a suppressive effect (see Figure 17). This is consistent with the iso-oriented collinear facilitation demonstrated with simple flanking lines (Kapedia et al., 2000) and low contrast stimuli (Chen & Tyler, 2008), as well as the suppression with high contrast iso-oriented collinear gabor flankers (Chen & Tyler, 2008; Cavenaugh et al., 2002). By comparison, Coen-Cagli et al. (2012) show that iso-orientated lateral surrounds have much weaker, and even neutral, effects. This is consistent with the neutral effect seen with simple iso-oriented lateral flanking lines (Kapedia et al., 2000) and neutral or suppressive effect from iso-oriented lateral flanking stimuli.

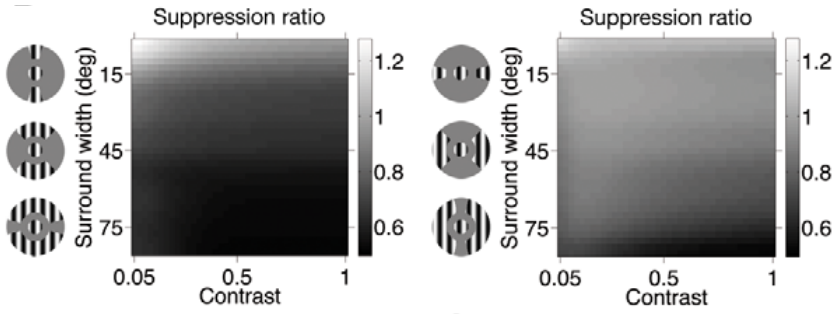

Figure 17. The spatial asymmetry of surround modulation. A suppression ratio above one indicates facilitation and below one indicates suppression. Left: Facilitation occurs for low contrast small collinear flankers. Suppression occurs for

larger and higher contrast collinear stimuli. Right: The effects are much weaker for most of the lateral stimuli. The strongest lateral suppression occurs when stimuli are high contrast and large. Figure taken from Coen-Cagli et al. (2012).

Most researchers seem to think that the collinear area is the main contributor to the surround effects (Field et al., 1993; Kapadia et al., 2000; Polat & Sagi, 1993; Schwartz et al., 2006). However, Mareschal and Clifford (2013) found that the area of surround stimuli driving the effect varied between individuals. They presented participants with STI surround stimuli that were made up of patches of both clockwise and counter-clockwise 15 degree tilts. Trial to trial, different parts of the surround contained either the clockwise or counter-clockwise components. They were able to extract which components were used to make a decision by summing the CW masks and the CCW masks for trials that the participant perceived the center stimulus as having a CW tilt, versus those trials where they perceived it as having a CCW tilt. They found that the areas affecting perception were not concentrated in the collinear regions as predicted. Rather, they found that each participant relied on a unique region, mostly near the outer edge of the center stimulus. This suggests that there are individual differences in the weighting of the modulation from specific regions of the surround. However, it is also possible that regional effects were washed out from the presence of both CW and CCW tilts of nearby regions, due to nonlinearities in the ways in which the effects may be combined.

In summary, the regions of the surround stimuli have different modulatory effects on the central stimulus. In most cases the collinear regions drive a facilitative neural effect and an attractive perceptual effect. However, the magnitude of this

effect will vary with the orientation and strength of the stimulus. For weak stimulation (i.e., simple flanking lines, orthogonal gabor orientations, or low contrast surrounds) the collinear region has a facilitative effect. However, when the stimuli are stronger (i.e., high contrast, iso-oriented) then the facilitative collinear region can actually switch to a suppressive collinear region. This has interesting implications for how we group and segment natural stimuli. Some researchers suggest that this collinear region is vital for connecting line segments into a single edge. However, this perceptual grouping may actually lead to attributing the center and collinear surround to the same gain pool, therefore yielding a larger repulsive effect as a way to reduce redundancies in the neural representations. The lateral regions typically appear to have a suppressive effect that may transfer to weak facilitation for low contrast orthogonal flankers. Not all surround stimuli can address the different modulatory effects of surround regions. The STI is typically a full surround, which may be a sum (or other combination) of the effects of the specific surround regions. We will keep this in mind as we further explore the relationship between center and surround.

Individual differences in spatial integration

Next, we will discuss individual differences in spatial integration.

Magnitude of context effects and orientation sensitivity

There is an interesting relationship between the magnitude of perceptual surround effects and orientation sensitivity (Song, Schwarzkopf & Rees, 2013). Individuals who are more sensitive to orientation changes are less susceptible to the influence of a 15-degree suppressive surround (Song et al., 2013; see Figure 18).

The authors propose that this relationship is a result of individual differences in the cortical surface area of V1. They reason that a larger visual cortex would lead to a larger representation of the stimulus, because more neurons would be involved in encoding the stimulus, making the person more sensitive to changes in that representation. Increased cortical surface area would also reduce the relative area for intracortical connections, which may not be able to scale with cortical size (that is, if the length of intracortical connections remain constant across individuals in spite of increased V1 surface area, these connections will have a relatively smaller reach). This relative reduction in the reach of horizontal connections could lead to a reduction in surround suppression. In fact, both orientation discrimination threshold and the magnitude of the contextual effect are negatively correlated with V1 surface area (but not V2 or V3) as measured by phase-encoded retinotopic mapping in fMRI.

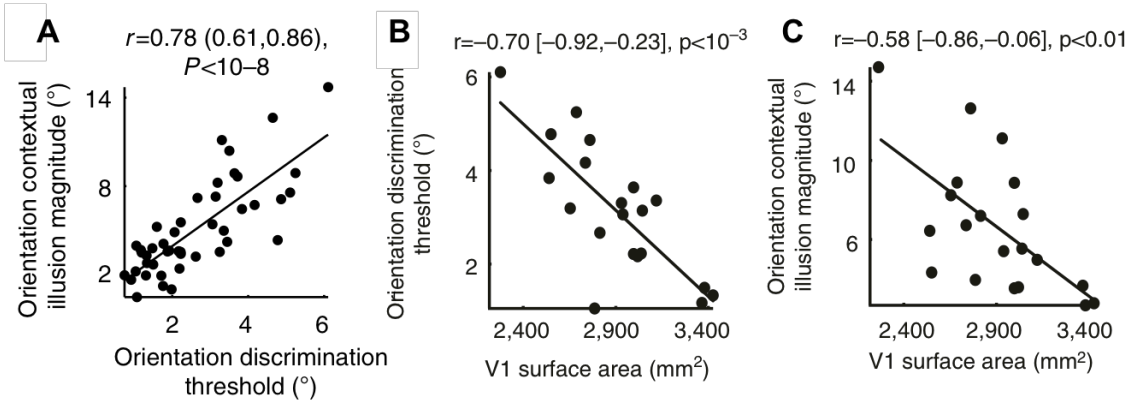

Figure 18. The relationship between orientation sensitivity, orientation specific perceptual surround suppression and V1 surface area. A) Subjects who are more sensitive to orientation are less susceptible to the context effects. Subjects who have a larger V1 surface area are B) more sensitive to orientation and C) less susceptible to the context effects. This figure was created from a combination of figures from Song et al. (2013).

This relationship can be explained by horizontal connectivity within V1. Song et al. (2013) found the same relationship between sensitivity and context effects using a simulation that varied in horizontal connectivity rather than cortical size. Song et al. (2013b) also show that individual differences in horizontal connectivity are correlated with the magnitude of the tilt illusion.

Clinical group differences in spatial integration

The relationship between the magnitude of the context effects and orientation sensitivity is also connected to traits related to Autism and Schizophrenia. People with schizophrenia show reduced surround contrast effects (Anderson et al., 2016; Dakin, Carlin and Hemsley, 2005; Kéri, Kelemen, Benedek, and Janka, 2005; Must, Janka, Benedek and Kéri, 2004). This is likely due to lower GABA levels in the visual cortex, which indicates weakened contrast gain control (Yoon et al., 2010; Yang et al., 2013). However, it is also possible that these group differences are partially due to differences in attention to the task (Barch et al., 2012). The differences also seem to be specific to contrast effects, with no difference in luminance or orientation surround effects (Yang et al., 2013). Although there was not group difference in orientation surround effects, symptom severity was positively correlated with the magnitude of the repulsive effect (Yang et al., 2013).

There is evidence that people with Autism are less susceptible to the influence of contextual stimuli (Happe & Firth, 2006) and have a local processing bias (Dakin & Frith, 2005). The weak central coherence theory (Happe & Firth, 2006) states that people with autism have a deficit in global processing. This is in contrast to the enhanced perceptual functioning theory (Mottron, Dawson,

Soulieres, Hubert & Burack, 2006), which states that people with autism have enhanced local processing. Both models predict that people with ASD will have decreased susceptibility to perceptual biases, as assessed using context-dependent illusions. However, the actual evidence supporting this is mixed, perhaps due to the complications associated with testing an ASD population and finding well-matched controls.

Another option is to search for correlations between perceptual biases and various autistic traits, which have been found to exist as a continuum in the general population (Wheelwright et al., 2006). These traits include the empathizing quotient (EQ, a measure of drive to recognize and respond to other's emotional state; Baron-Cohen & Wheelwright, 2004), the systemizing quotient (SQ, a measure of the drive to analyze, understand, predict, control and construct rule-based systems; Baron-Cohen, Richler, Bisarya, Gurunathan, & Wheelwright, 2003), and the Autism Quotient (AQ, which is a broadband measure of individual differences in traits related to Autism; Baron-Cohen, Wheelwright, Skinner, Martin & Clubley, 2001). People with autism tend to score at the extreme ends of the continua, with high SQ and AQ scores and low EQ scores.

There is also evidence that neurotypical individuals who score high on AQ and SQ perform better on tasks that require ignoring contextual information (such as the embedded figures task) than do individuals who score low on these traits (Almeida et al., 2010, see Figure 19 for an example of an embedded figures stimulus). They are also less susceptible to the influence of contextual illusions (SQ, Walter, Dassonville & Bochsler, 2009). High SQ (but not AQ) is associated with a

decrease in some types of context effects, including the rod-and-frame, Roelofs, Ponzo and Poggendorff illusions (Walter et al., 2009). However, scoring high on a subscale of the SQ, Insistence on Sameness (IS), is associated with increased local contrast effects (Reed & Dassonville, In Progress). There is also evidence that people who score high on AQ show decreased surround suppression (Flevaris & Murray, 2015) and increased orientation sensitivity (Dickinson, Jones & Milne, 2014).

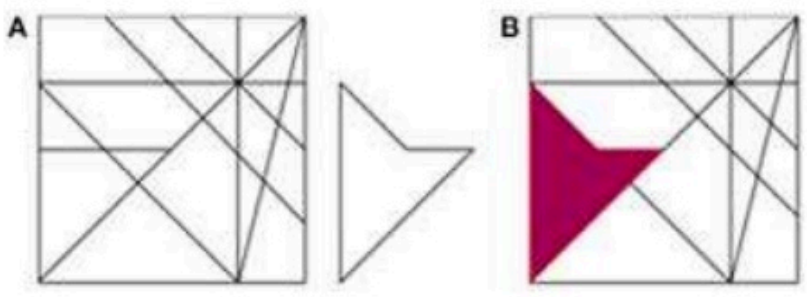

Figure 19. Example of the traditional Embedded Figures Task.

The increase in orientation sensitivity for people who score high on traits related to autism may be related to the balance between inhibitory and excitatory responses (Rubenstein & Merzenich, 2003; Snijders, Milivojevic & Kemner, 2013), as indicated by the amount of the inhibitory neurotransmitter GABA. Edden, Muthukumaraswamy, Freeman, and Singh (2009) found that orientation detection thresholds were inversely related to resting GABA in the visual cortex. This means that people who showed more orientation sensitivity had higher concentrations of GABA in their visual cortex. Another indication of the excitatory and inhibitory balance within individuals is the oscillatory gamma response, which is positively correlated with GABA in the visual cortex and with orientation sensitivity (Edden et al., 2009).

Given these relationships between autistic traits and orientation selectivity, and between orientation sensitivity and GABA, we may expect, at first glance, that people with autism would have higher concentrations of GABA and increased gamma oscillations because they show increased orientation sensitivity. However, the literature on this tends to show that people with autism have reduced, or similar levels of GABA in the visual cortex as the typically developing population (Gaetz et al. 2014; Robertson, Ratai & Kanwisher, 2016). In fact, it is thought that an elevated ratio of excitatory to inhibitory responses would lead to some of the social and perceptual impairments seen in autism (Rubenstein & Merzenich, 2003). Consistent with this hypothesis, Snijders et al. (2013) found that people with autism showed less gamma power in EEG recordings of the visual cortex during the presentation of surround stimuli compared to control subjects. This could be an indicator that the group with autism experienced less suppression from the surround stimulus. There is also evidence that people who score high on AQ have reduced surround suppression as indicated by a difference in BOLD response to iso-oriented and orthogonally-oriented surrounds (Flevaris & Murray, 2015).

A reduction in surround suppression and an elevated excitatory to inhibitory response ratio in autism can be modeled with divisive normalization (Rosenberg, Patterson, & Angelaki, 2015). Rosenberg et al. (2015) determined the activity of a population of model neurons by computing the response of a model neuron at position X and with sensitivity to orientation, Θ:

$$R(X,\theta) = \frac{D(X,\theta)}{v + c * S(X,\theta)}$$

where D is the driving signal of the target neuron and S is the weighted sum of driving signals from neurons in the suppressive field. The semisaturation constant, v, determines the rate at which the neural response will reach its maximum response rate. The gain term, c, determines the neuron's sensitivity to the context information. It scales the suppressive field input so that a small gain term will lead to less suppression. To model autism, the authors reduced the gain term by 25%. They found that this reduction in the gain term led to reduced surround suppression for visual context stimuli in the "ASD" model neurons. The gain term was set as a constant here but it could also be a function of tuning properties with experience (Schwartz & Coen-Cagli, 2013). That is, prior experience with natural scenes will tune responses as a way to optimize neural coding. It is possible that people with autism do not rely on prior experience as much as the typically developing population.

In summary, there is evidence that people with autism, as well as neurotypical individuals who score high on traits related to autism, have increased orientation sensitivity and decreased surround suppression. Some researchers attribute these relationships to an increased ratio between excitation and inhibition. While this hypothesis does not directly predict an increase in sensitivity, it does predict the reduced surround effects. Although, greater Insistence on Sameness is correlated with an increase in local contrast effects. Reduced surround effects are also predicted by a computational account that proposes that people with autism may be less likely to use prior experience with natural scene statistics and therefore use less contextual information when processing visual information

Within subject state effects on spatial integration

In addition to between-subject differences in spatial integration, there is also evidence that the extent to which surround information influences perception of a central target is dependent on state differences within a subject. During attentive and alert brain states cortical gain increases and surround effects are reduced.

An indicator of brain state or cortical gain in animals is activity level of the subject. It is known that visual responses increase with locomotion (Bennett, Arroyo & Hestrin, 2013; Niell & Stryker, 2010). Ayaz, Saleem, Scholvinck, and Carandini (2013) show that locomotion also affects spatial integration. The authors recorded neurons in the primary visual cortex from head fixed mice placed on a spherical treadmill. They found that there was strong surround suppression when the mice were stationary. However, surround suppression decreased during locomotion.

Typically the neural response to a stimulus increases with stimulus size up to an optimal point at which the stimulus goes beyond the driving field and impinges onto a suppressive surrounding field. Here, neural responses did not drop off with increase in stimulus size when the mice were moving. This effect looks a lot like a response gain change. When Ayaz et al. (2013) model the results with a simplified gain normalization model, Response = Baseline +(Drive/Suppression), they found that locomotion caused the baseline activity level to increase as well as the Drive/Suppression ratio. In some neurons, that ratio increase was due to an increase in drive; in others, it was because of a decrease in suppression. The size of the summation area was larger when mice where moving than when they were stationary.

Importantly, Ayaz et al. (2013) suggest that the effect of locomotion is not due to increased spatial attention. Spatial attention to both the center and surround would lead to more surround suppression, not less (Schwartz and Coen-Cagli, 2013). The effect of locomotion also appears to be different from the modulatory effects of injected ACh. Roberts et al. (2005) show that the summation area is reduced with ACh, which is naturally released with attention and arousal. It is possible that the locally-injected ACh was more than would be naturally released with increased cortical gain. Too much stimulation could actually lead to a reduction in summation area. It is also possible that the modulatory effects of locomotion are not related to increases in ACh, but are instead related to the phasic activation of the locus coeruleus norepinephrine (LC-NE) system (Neves, van Keulen, Yang, Logothetis, & Eschenko, 2017).

In summary, there are several individual differences, as well as within-individual differences, that can modulate spatial integration. People who are more sensitive to orientation also tend to have reduced surround suppression. This relationship may be driven by individual differences in cortical size. An increase in orientation tuning and a decrease in surround suppression are also associated with increased cortical gain. Increased cortical gain may be from neural increases in baseline firing rate or excitatory responses, decreases in inhibitory responses or from individual differences that lead to reduced weighting of the gain control response.

Discussion

In this chapter, I reviewed and synthesized the literature pertaining to orientation specific spatial integration. I focused on how neural and perceptual responses to orientation were moderated by the presence of a surrounding stimulus. Neurons responding to the surround stimuli send inhibitory and excitatory inputs to the neurons responding to the center stimulus. These responses lead to a suppressive or facilitative effect. Populations of neurons responding to a central stimulus will have a distribution of responses around the orientation of the central stimulus. The peak of this distribution may be shifted by the suppressive and facilitative inputs to these neurons. When the peak shifts, the overall perception of the orientation of the central stimulus shifts, yielding perceptual repulsion or attraction.

Perceptual surround effects are induced with several types of stimuli, as precise as a single line and as extensive as a full STI surround. The full STI surround induces a repulsive effect when its relative orientation is about 15 degrees from the central stimulus' orientation. This effect can be described by divisive normalization that manifests through lateral inhibition. Lateral inhibition occurs when neurons that respond to the surround stimulus send horizontal connections to inhibitory interneurons that suppress neurons whose receptive field is in the same spatial position as the center stimulus and has the same orientation preference as the surround stimulus. The normalization process helps to reduce redundancies in neural coding, but it also can lead to an illusory shift in orientation perception.

This process can also lead to a perceptual attraction effect when similarly tuned cells that are perceptually segmented from the central stimulus are weakly grouped in the normalization pool. This may be driven by lateral disinhibition, which can produce a surround facilitation effect. Here, there is inhibition between neurons with different orientation preferences that sample from the same location. This leads to the release from inhibition coming from neurons with the same orientation preference. The surround induces an attractive effect when there are large differences in the relative orientation of the center and surround (around 75 degrees). This attractive effect is much smaller than the magnitude of the repulsive effect. Because disinhibition is based on the effects of inhibition, the facilitative effects will always be predicted to be smaller than the suppressive effects.

However, lateral connections alone cannot account for the extent of all surround effects. They are too slow and spatially limited to be able to produce all contextual effects. We can identify the impact of lateral connections by physically (e.g., a gap) or perceptually (e.g., different colors) segmenting the center and surround. This reduces surround effects. It is also likely that feedback connections play a role in surround effects. However, there is mixed evidence about which types of surround effects are driven by feedback connections. Some researchers think that feedback connections drive all of contrast facilitation (Polat and Sagi, 1993, 1994). Another view is that feedback connections account for all perceptual attractive effects (Wenderoth & Johnstone, 1988; Smith and Wenderoth, 1999). While that may be an extreme view, there is evidence that feedback connections drive contrast facilitation from laterally positioned stimuli (Cass and Spehar, 2005) and that they

contribute to iso-oriented surround suppression (Bair, Cavanaugh and Movshon, 2003).

It seems likely that surround effects are caused by a combination of lateral and feedback connections, and different effects will arise depending on the precise methods for testing them. For example, if you are testing the relative effect size driven by feedback verses lateral connections by looking at how the effects are modulated over time, early effects of feedback may obscure the slower effects of horizontal connections. It is also possible that the inhibitory and excitatory connections will be affected differently by the stimuli used to test for horizontal connections. It is thought that the inhibitory connections have a higher threshold of activation than the excitatory connections (Chen & Tyler, 2001; 2008; Kim and Freeman, 2014; Schwabe et al., 2006; Stemmler et al., 1995; Weliky et al., 1995). If the surround stimulus is reduced in size, it may reduce the impact of the inhibitory effects but not the excitatory effects. This would lead to the appearance of a gap-induced reduction in lateral inhibitory effects. If the facilitative effects appeared to not be impacted then it could be assumed that they stemmed from feedback connections.

There are different areas of the surround that lead to facilitative and suppressive effects. In most cases the collinear regions in the surround drive a facilitative neural effect and an attractive perceptual effect. Kapedia et al. (1999) state that these effects are from direct excitatory connections. The magnitude of sensory input will move the effect from facilitative to suppressive, at least for contrast perception. It is a little less clear how orientation perception will shift by

varying the strength of stimuli from different regions. For iso-oriented collinear line flankers there is a facilitative effect (Kapedia) but for iso-oriented collinear gabor flankers there was a primarily suppressive effect (Cavanaugh, Bair and Movshon, 2002). This suggests that there are subthreshold inhibitory connections for the line flankers that reach suprathreshold levels with the gabor flankers. The same is possibly true for orthogonally-oriented lateral flankers. They have a primarily weak suppressive effect when presented as gabors, but a small facilitative effect when presented as lines.

We can think of facilitation and suppression as responses with different activation thresholds that lay on a continuum. Rather than thinking of a specific surround region as being the "facilitative region" it may be useful to think of the regions as having more or less inputs to the central response. If the weights of surround inputs are tuned with exposure to natural scene statistics, then we would expect there to be more connections at the collinear regions. Therefore, the regional position and strength of the surround stimulus will determine the magnitude and direction of the surround effect. In our first study, we determine the extent to which prior experience with natural scenes determines the extent to which different surround regions will be integrated. We also address potential differences in the regional integration mechanisms.

It is thought that the relationship between regional surround effects and sensitivity is mediated through horizontal connectivity. People who are more sensitive to orientation tend to have reduced surround suppression and larger cortical surface area. This relationship is based on the assumption that people with

a large visual cortex will have reduced horizontal connectivity between hypercolumns. Again, we may expect to see this relationship more for collinear surround effects because the collinear position may have stronger/more lateral connections.

There are individual differences that will modulate surround effects. People with autism and schizophrenia show reduced surround suppression. Some of these perceptual disruptions can be described by reduced gain control. If someone relies less on prior knowledge of natural scene statistics to efficiently process visual information then they will show reduced gain normalization. It is unclear how these individual differences will impact the effect of surround regions. It is possible that these individual differences in surround effects would be seen most for the collinear surround regions because effects from these regions rely on a strong smoothness prior. In our second study, we determine the extent to which autistic traits are associated with changes in orientation sensitivity and spatial integration. This has potential implications for understanding changes to integration mechanisms in disorders that have disrupted perception.

The increase in orientation tuning and a decrease in surround suppression are also associated with increased cortical gain within subjects. In Study 3 we determine the extent to which spatial integration is modulated by natural fluctuations in internal arousal states. Here, we measured the amount of perceptual repulsion caused by an oriented surround for cases of low and moderate arousal, as indexed by pupil size.

There is still much of spatial integration that needs to be understood. A model of flexible divisive normalization provides a framework for understanding how stimulus strength, orientation and region lead the perceptual integration of the surround stimulus. It can also provide insight into individual variations in a generalized computation. Importantly, this framework can make predictions about perceptual effects without committing to a specific neural mechanism. The goal of this work is to provide insight into the types of neural connections involved with spatial integration and understand how connectivity changes to account for prior experience.

CHAPTER 2: COLLINEAR AND LATERAL REGIONS OF THE SURROUND ARE INTEGRATED DIFFERENTLY

In our first study, we measure how orientation perception is affected by surround regions with different probabilities of coassignment to the center (i.e. lateral vs collinear). Our goal is to understand how prior experience with natural scenes determines the extent to which different surround regions will be integrated. We also address potential differences in the regional integration mechanisms.

Background

Spatial integration can be studied using perceptual illusions that occur when contextual information within the area around a target biases perception of that target. The influence of the surrounding stimuli on the perception of a target's orientation is well established using the Simultaneous Tilt Illusion, STI (See Figure 20; Clifford, 2014; Gibson & Radner, 1937; Westheimer, 1990). The STI is a situation in which a surrounding stimulus biases the perceived orientation of a simultaneously presented central test stimulus. The angular difference between the orientations of the inducing and test stimuli determines the magnitude and direction of the illusion. In the case of the STI, a repulsive effect means that the perceived orientation of the center will be biased in the direction opposite the surround. The strongest repulsive effect happens where the difference between the angle of the center and surround is 10-20 degrees. The strongest attractive effect, a bias towards the orientation of the surround, occurs when there is a relative difference of 75-80 degrees.

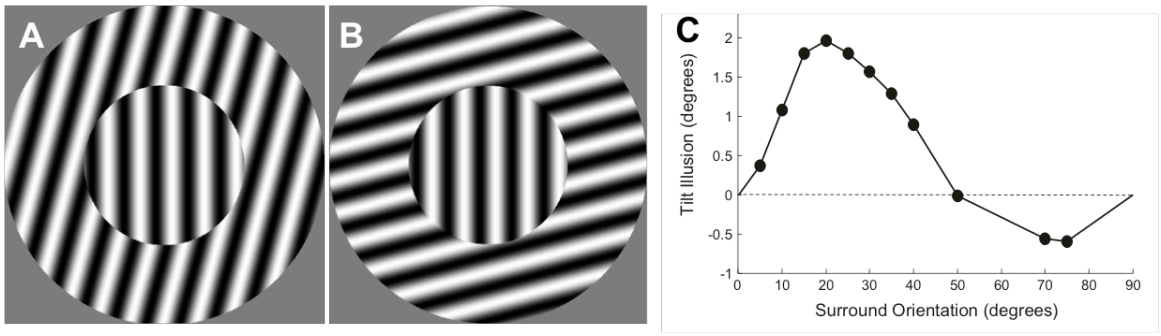

Figure 20. Example of (A) perceptual repulsion and (B) perceptual attraction of an oriented stimulus to the surround. The magnitude of the illusion changes with relative orientation of the center and surround (C, taken from Clifford, 2014).

The tilt illusion manifests when neurons that respond to the center stimulus are modulated by neurons that respond to the surround stimulus. The classical receptive field (CRF) is an area in the visual field to which a neuron is directly sensitive (Hubel & Wiesel, 1968). The CRF is stimulated through feedforward connections that are hierarchical and send information about a stimulus up through successive levels of processing in the visual system, starting from the eye. Originally, scientists thought that a neuron's response to a stimulus in its CRF was independent of the responses from other neurons (Hartline & Graham, 1932). However, the response to stimuli in the CRF can be modulated by neighboring neurons when surrounding information is present (Allman, Miezin, & McGuinness, 1985; Blakemore & Tobin, 1972; Cavanaugh, Bair and Movshon, 2002; Gilbert & Weisel, 1990; Kapadia et al., 1995; Knierim & van Essen, 1992; Levitt and Lund 1997; Maffei & Fiorentini, 1976; Nelson & Frost, 1978). The CRF response can be modulated by feedback from extrastriate areas (Hupé et al., 1998) or through horizontal connections between nearby cells in the visual cortex (Hirsch and Gilbert, 1991). Although both feedback and horizontal connection are involved in spatial

integration, horizontal connections seem to drive the orientation specific effects that are seen with the tilt illusion (Kim & Freeman, 2014).

In addition to the STI, there are several other types of visual stimuli that experimenters use to induce perceptual surround effects. Each stimulus yields slightly different effects. In fact, spatial position of the contextual stimulus will determine the magnitude and direction of the tilt effect (Chen & Tyler, 2008; Coen-Cagli, Dayan & Schwartz, 2012; Kapedia, Westheimer, & Gilbert, 2000; Mizobe et al., 2001; Qiu, Kersten, & Olman, 2013; Schwartz, Sejnowski, & Dayan, 2006). For example, surround stimuli positioned collinearly (i.e., at the endpoints of the lines of the center stimulus; See Figure 21, A) can have a different effect than surround stimuli positioned laterally (i.e., to the sides of the lines of the center stimulus; Figure 21, B).

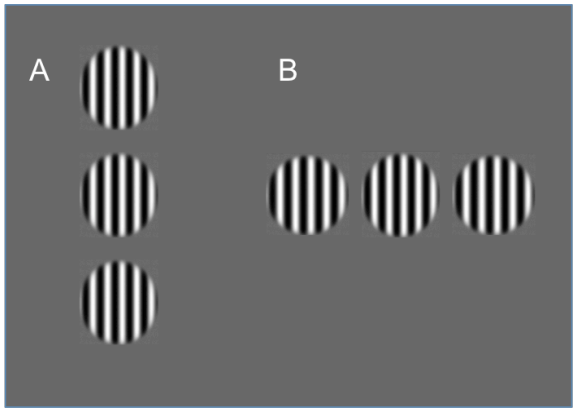

Figure 21. Example drawing of (A) surround stimuli positioned collinearly to the center stimulus, and (B) surround stimuli positioned laterally to the center stimulus.

The effect of the surround in different stimulus configurations can be predicted by a model of divisive normalization. Normalization occurs when a neural response is divided by a common factor that is the summed activity of a pool of neighboring neural responses (Carandini & Heeger, 2012). This division helps to

reduce redundancies in perceptual processing. A flexible model of divisive normalization accounts for cases in which the center and surround are part of the same object and cases when they are part of different objects. When they are co-assigned to the same object the center and surround activations will be dependent. The center is only normalized by the surround when they are co-assigned to the same object (Coen-Cagli, Dayan & Schwartz, 2012; Schwartz et al., 2009). The probability that the center and surround are co-assigned is determined by their feature similarity (here, the focus is on orientation, but other relevant features could include contrast, color, spatial frequencies, etc.). In the full model, the output is the average of the two cases (normalization and co-assigned or not normalized or co-assigned) weighted by their probability. Therefore, the cortical output of the model is a Bayesian estimate of the local distributions given the dependencies between them.

Relative orientation isn't the only thing that affects probability of co-assignment. Another factor is the spatial position of the surround. Center and surround units tuned to natural scene statistics will have a higher probability of co-assignment when the surrounds are positioned collinearly to the center stimulus than surrounds positioned laterally (Coen-Cagli, Dayan & Schwartz, 2012). Therefore, surround effects will be larger when surrounds are collinearly positioned.

Regional contributions to the full surround effect

Given that the collinear surround position has a higher prior probability of co-assignment with the center means that the collinear surrounds will modulate the

center responses more than the lateral surrounds (Coen-Cagli et al., 2012). This modulation is dependent on stimulus strength (i.e. stimulus size and contrast). Iso-oriented collinear simple flanking lines (Kapedia et al., 2000) and low contrast collinear flanking gabors (Chen & Tyler, 2008) have a facilitative effect. However, high contrast iso-oriented collinear gabor flankers have a suppressive effect (Chen & Tyler, 2008; Cavanaugh et al., 2002). Coen-Cagli et al. (2012) model these effects and show that weak iso-oriented collinear surrounds drive a facilitative effect while strong iso-oriented collinear surrounds drive a suppressive effect. Simple iso-oriented lateral flanking lines (Kapedia et al., 2000) and lateral flanking gabors (Chen & Tyler, 2008) have neutral or weakly suppressive effects. Coen-Cagli et al. (2012) model these effects and show that iso-orientated lateral surrounds have much weaker, and even neutral, effects.

What is currently unknown is the extent to which the collinear and lateral regions of the full surround STI stimulus contribute to the overall surround effect. It is also unclear if the regional influence will vary for perceptual repulsion and perceptual attraction. If divisive normalization tuned to natural scene statistics were the mechanism producing the effects then we would predict that the collinear region would drive the overall effect. This should be true for both perceptual repulsion and perceptual attraction. Based on the modeling of Coen-Cagli et al. (2012), we predict that the collinear position will be associated with larger effects of the surround regardless of the direction of the effect (attractive or suppressive).

Regional Connectivity

There is an interesting relationship between the magnitude of perceptual surround effects and orientation sensitivity (Song, Schwarzkopf & Rees, 2013). Individuals who are more sensitive to orientation changes are less susceptible to the influence of a 15-degree suppressive surround (Song et al., 2013). The authors propose that this relationship is a result of individual differences in cortical surface area. They reason that a larger visual cortex would lead to a larger cortical representation of the stimulus (that is, more neurons would be involved in encoding the stimulus), resulting to greater sensitivity to changes in that representation. Increased cortical surface area would also reduce the *relative* reach of intracortical connections, which may not be able to scale with cortical size. This reduction in horizontal connections could lead to a reduction in surround suppression. In fact, both orientation discrimination threshold and the magnitude of the contextual effect are negatively correlated with V1 surface area (but not V2 or V3) as measured by phase-encoded retinotopic mapping in fMRI.

Song et al. (2013) simulated the relationship they found between sensitivity and context effects by varying horizontal connectivity with cortical size. This simulation showed that horizontal connectivity within V1 may explain the relationship between individual differences in surround effects and orientation sensitivity. This is supported by fMRI studies showing that intrahemispheric connectivity in V1 is correlated with the magnitude of the tilt illusion (Song et al., 2013b; Song & Rees, 2018) and that cortical surface area is correlated with orientation sensitivity (Song, Schwarzkopf, Kanai & Rees, 2015). Together these

results indicate that the relationship between orientation sensitivity and the magnitude of the tilt illusion is related to individual differences in horizontal connectivity.

Horizontal connectivity between the center and surround may vary with surround regions. Lacaruso, Gasler and Hofer (2017) found that there is more connectivity between receptive fields that are co-axially aligned and co-oriented with the center receptive field. The number of connections between co-axially aligned receptive fields decreased as the orientation deviated from the orientation preference of the center receptive field. Laterally aligned receptive fields had fewer connections to the center receptive field and the number of connections did not depend on orientation preference. This demonstrates increased connectivity between receptive fields representing regions of space that have a higher probability of being co-oriented and, therefore, part of the same edge.

Assuming that horizontal connectivity is the mechanism that drives the relationship between sensitivity and context effects then we would expect that the surround region that relies on these intrinsic connections the most would have the strongest correlation between sensitivity and context effects. If the prior probability of strong collinear effects were due to an increase in the connectivity between intrinsic orientation specific neurons then we would predict that the collinear surround effects would be strongly correlated with sensitivity. However, if the horizontal connectivity were the same for all regions we would predict no regional differences in this relationship.

We hypothesize that the collinear surround will contribute to the overall magnitude of the STI more than the lateral surround region. We also hypothesize that orientation sensitivity will be most strongly correlated with the collinear surround effects of the tilt illusion.

Methods

To test these hypotheses we compared the illusory effect of the full STI to the effect driven by surrounding contexts limited to isolated collinear and lateral regions, with orientation sensitivity additionally measured with no surround. These effects were measured using a two alternative forced choice task, which was created using PsychoPy2 Experiment Builder (v1.84.2; Peirce, 2009).

The experiment took place in a small, darkened room, with walls painted a flat black. All stimuli were presented on a 27" Apple Mac Pro with a resolution of 2560 x 1440 pixels. A black circular mask was placed over the monitor so that the edges of the monitor could not be used as orientation references.

Participants

225 participants (110 in Experiment 1 and 115 in Experiment 2) volunteered in exchange for course credit or a $10 payment. A power analysis of the data from Song et al. (2013) revealed that we would only need 14-27 subjects to see a correlation comparable to that observed between the full surround effect and orientation sensitivity.

Stimuli

Stimuli (Figure 22) were based on those used by Song et al. (2013). All stimuli were presented on a grey 50% luminance background. The center was an oriented sinusoidal grating (3 cycles/dva) with a hard aperture that measured 1.5 dva. The full surround was a sinusoidal grating (also 3 cycles/dva) in a circular annulus with a soft aperture, which was used to reduce a potential global orientation effect with the lateral and collinear surrounds (see below). The soft aperture was created using a Gaussian with a standard deviation of .75 dva. We included a multiplier to keep 1.5 SD's at full contrast. This allowed the surround to have full contrast beyond the area of central stimulus and then fade at the edges of the surround.

The lateral and collinear surrounds were narrow ellipses, which only covered the lateral and collinear regions outside of the center, respectively. The widest point of the ellipses matched the diameter of the full surround. The ratio of the distance between the narrowest and widest points of the ellipse was 1:2.5.

In Experiment 1, the surrounds were oriented either 15 degrees clockwise (CW) or counter-clockwise (CCW) from the reference orientation (45 degrees). On average, this orientation leads to perceptual repulsion for the full surround conditions. In Experiment 2, the surrounds were oriented either 75 degrees CW or CCW from the reference orientation. On average, this orientation leads to perceptual attraction for the full surround conditions. There were 7 conditions in each experiment: 3 surround shapes (full, lateral, or collinear) x 2 surround orientations (Exp. 1: 15 degrees CW or CCW; Exp. 2: 75 degrees CW or CCW) + no surround (1).

On each trial, participants were presented with a sequential set of stimuli: a reference and a probe. The reference was always a 45-degree center stimulus with no surround. The probe was a center stimulus that was either alone or accompanied by a surround depending on the condition. The probe configuration was pseudo-randomly chosen from the seven stimulus conditions described above.

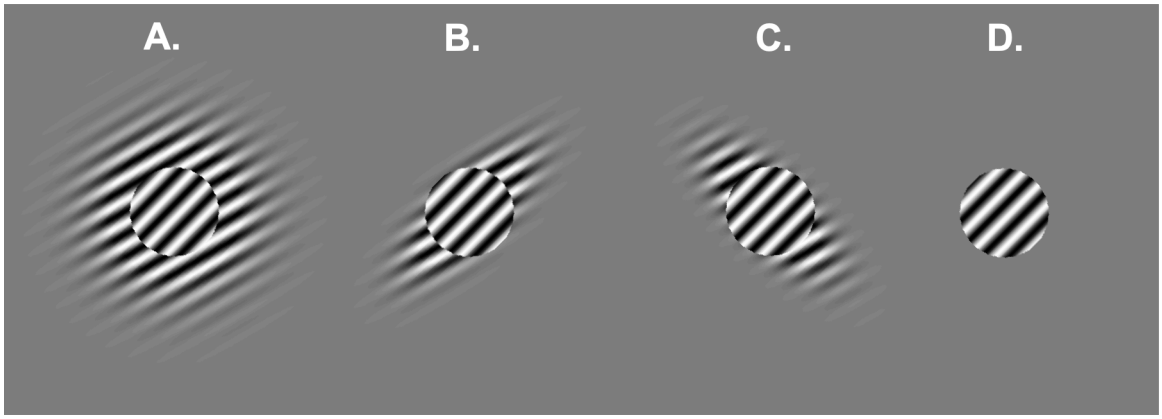

Figure 22. Example drawing of probe stimuli with (A) full surround, (B) collinear surround, (C) lateral surround, and (D) no surround. (A-C) The surrounds in these examples are 15 degrees CCW from the reference orientation of 45 degrees.

Procedure

Participants initiated the start of each trial by pressing the space bar. This triggered the presentation of a red fixation point for 1000 ms. Then the first stimulus (reference or probe, with order randomized on each trial) was presented for 300 ms, followed by a small white fixation point for 500 ms, and then the presentation of the second stimulus for 300 ms. Participants were asked to compare the relative orientations of the reference and probe, pressing a left button to indicate that the second stimulus was rotated CCW from the orientation of the first, or a right button to indicate that the second was rotated CW from the first. After

they pressed the response key, participants advanced to the next trial by pressing the space bar.

The orientation of the probe was determined using a staircasing procedure. There were two interleaved staircases for each stimulus condition: one starting with a probe angle that was rotated 15-degrees CW from the reference angle, and the other starting with a probe angle that was rotated 15-degrees CCW from the reference angle. When the previous response to a trial in the staircase was correct the orientation of the probe was adjusted to be more difficult (i.e., closer to the reference angle of 45 degrees). When it was incorrect the probe was adjusted to be easier (i.e., further from the reference orientation). Thus, the staircase procedure caused the perceived orientation of the probes to converge toward the reference orientation.

To measure sensitivity, two incorrect responses were required to make the next trial in the no-surround condition easier, but only one correct to make it more difficult. This led the staircases to converge on the orientation at which the participant reported the probe to be CCW of the reference on 70.7% of trials.

In all conditions, the initial step size of the staircase was 8 degrees. This step size was reduced to 4 degrees after the first reversal, to 2 degrees after the second reversal, and to 1 degree after the fourth reversal. Each staircase had a minimum of 20 trials, and ended after 18 reversals.

Participants completed 14 practice trials before starting the experimental trials. The practice trials were slower to allow the participant to become comfortable with the task (500 ms presentation time).

Control Study Methods

There was some concern that the contrast polarity between the center and surround would cause the collinear surround to appear more perceptually segmented than the lateral surround. If this were the case we would predict that the effect of the collinear surround would be smaller than the effect of the lateral surround. That is not the case. However, to control for possible differences in segmentation cues we ran a control study that was identical to Experiment 1 except that a grey annulus (0.2 dva) separated the center and surround, such that both stimulus types were perceived to be equally segmented. Thirty subjects participated for course credit.

Analysis

We averaged the orientation at the last ten reversals using trials from both staircases (probes starting CW or CCW of 45 degrees). This value described the point at which the staircases converged. For each surround condition, this was the point of subject equality (PSE), or the point at which the center probe and reference appear to be the same orientation. For the center alone condition, the staircases converged at the point at which participants were 70.7% correct.

The effect of each surround region was determined by identifying the difference between the PSE for the CW and CCW versions of the surrounds and dividing by two. This was calculated separately for each stimulus configuration for each subject. We calculated sensitivity threshold by taking the difference between the reference point (45 degrees) and the point at which participants were 70.7% correct. We defined sensitivity as the inverse of the sensitivity threshold. One

participant was removed from Experiment 1 and one participant was removed from Experiment 2 because we were unable to compute their orientation sensitivity when the staircases failed to converge.

Results

Experiment 1 (15 degree surround)

In Experiment 1, the 15 degree surround led to a significant repulsive shift in perception of the center for all surround configurations (Figure 23). The full surround had the largest repulsive effect (mean = 6.03, SD = 1.52, $t(108)=41.48$, $p<.01$), followed by the collinear surround (mean = 4.76, SD = 1.43, $t(108)=34.68$, $p<.01$) and then the lateral surround (mean = 3.74, SD = 1.29, $t(108)=30.27$, $p<.01$). A repeated measures ANOVA indicated that there was a significant effect of surround configuration, $F(2, 216)=171.54$, $p<.01$. A Tukey contrast indicates these effects were all significantly different from each other (*p adjusted*<.01 for all comparisons).

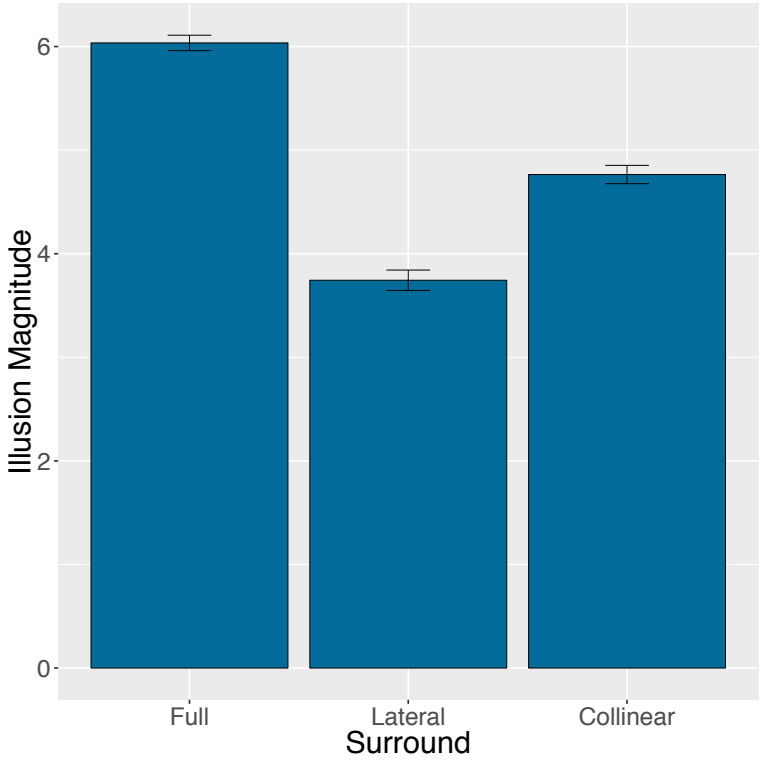

Figure 23. The mean shift in perception of the center under each surround configuration condition. Positive numbers indicate a repulsive effect. Error bars indicate within-subject standard error.

Next, a stepwise linear model was used to determine the extent to which each regional surround condition predicted the effect of the full surround. A linear model with only the collinear surround effect predicted the full surround effect (B = 0.76, r_2 = 0.51, $F(1,107) = 114.3$, $p<.01$). A linear model with both collinear and lateral surround effects significantly predicted the full surround effect (B_{col} = 0.60, B_{lat} = 0.41, r_2 = 0.61, $F(2,106) = 85.46$, $p<.01$). Although the beta weight was higher for the collinear surround alone, adding in the lateral surround to the model accounted for significantly more variance than the collinear model alone ($F(1,106)=27.89$, $p<.01$). Adding sensitivity into the model did not account for more variance than the model with both lateral and collinear effects (B_{col} = 0.60, B_{lat} =

0.41, B_{sens} = 0.03, r_2 = 0.61, $F(3,105) = 56.44$, $p<.01$; model comparison ANOVA $F(1,105)= 0.01$, $p=.94$).

We ran Spearman correlations to determine the relationship between orientation sensitivity and the magnitude of the repulsive effect of each surround condition (Figure 24). As predicted, based on the effects of Song et al. (2013), there was a significant negative correlation between sensitivity and the effect of the full surround ($r(107)=-0.36$, $p<.01$). As sensitivity increased across subjects, the effect of the full surround decreased. There was also a significant negative correlation between sensitivity and the effect of the lateral surround ($r(107)=-0.41$, $p<.01$). The correlation between sensitivity and the collinear surround was weaker but present ($r(107)=-0.24$, $p=.01$). These effects are still present even when we removed outlier participants (sensitivity over 3 standard deviations from the mean).

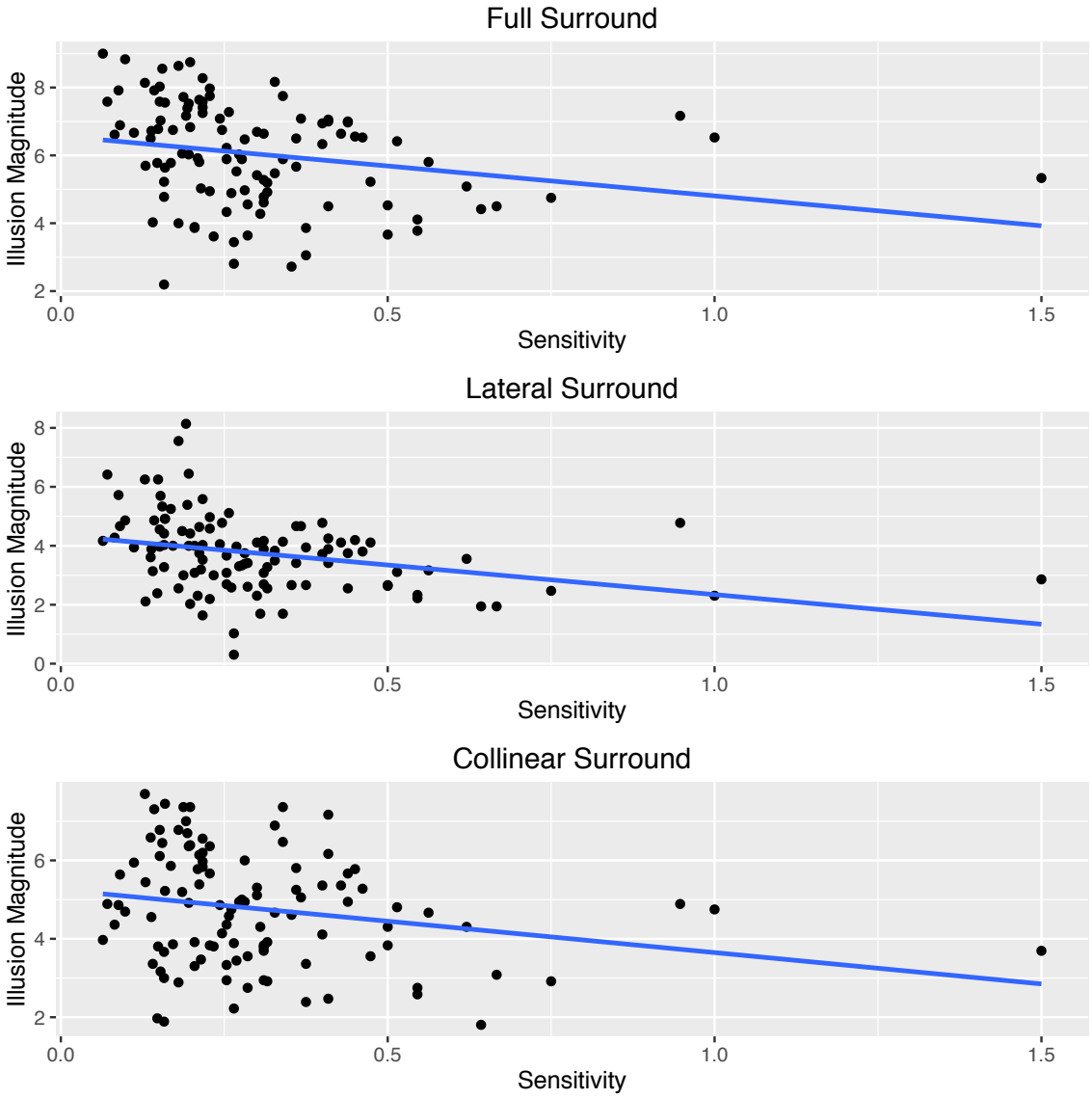

Figure 24. The relationship between orientation sensitivity and repulsive surround effects.

Control

The overall pattern of results for our control study was the same as that in Experiment 1, with the exception that none of the surround effects were significantly correlated with orientation sensitivity. This suggests that the correlation between the STI surround effect and orientation sensitivity described in Song et al. (2013) may not be as robust of an effect as previously thought (i.e. a

power analysis indicates that a minimum of 14 subjects would be required to observe this relationship). Using the results from Experiment 1 a power analysis indicates that we would actually need 57 subjects to observe the relationship. Therefore, it is highly likely that we do not observe this relationship because of low power and not because of the addition of the gap.

The 15 degree surround in the control led to a significant repulsive shift in perception of the center for all surround configurations (Figure 25). The full surround had the largest repulsive effect (mean = 5.27, SD = 2.10, $t(29)=13.72$, $p<.01$), followed by the collinear surround (mean = 4.42, SD = 1.86, $t(29)=13.02$, $p<.01$) and then the lateral surround (mean = 2.87, SD = 2.27, $t(29)=6.92$, $p<.01$). A repeated measures ANOVA indicated that there was a significant effect of surround configuration, $F(2, 87)=10.26$, $p<.01$. A Tukey contrast indicated that the collinear and full surround effects were not significantly different from each other but that they were both significantly larger than the effect of the lateral surround (*p adjusted*<.01). Consistent with Experiment 1, we found that the best model to predict the full surround effect was a combination of both the collinear and lateral surround effects ($B_{col} = 0.35$, $B_{lat} = 0.53$, $F(2,27) = 26.38$, $p<.01$).

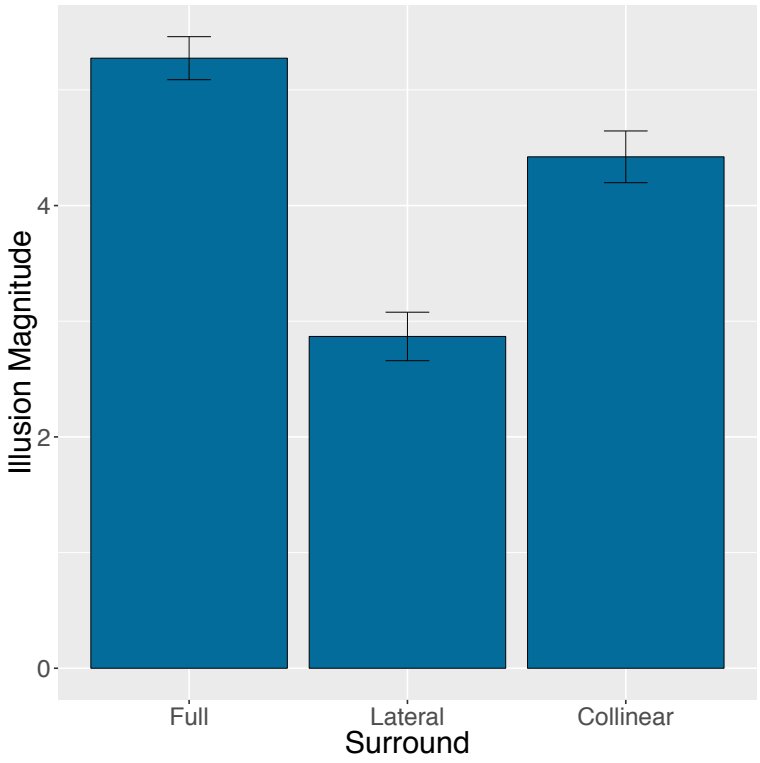

Figure 25. The mean shift in perception of the center under each surround configuration condition with a 15-degree surround tilt and a annular gap for the control study. Error bars indicate within-subject standard error.

Experiment 2 (75 degree surround)

In Experiment 2, the 75 degree surround led to a significant attractive shift in perception of the center for all surround configurations (negative effect sizes, Figure 26). The largest attractive effect came from the lateral surround (mean = -1.63, SD = 1.76, $t(113)=-9.91$, $p<.01$). The collinear (mean = -0.53, SD = 1.34, $t(113)=-4.23$, $p<.01$) and full (mean = -0.85, SD = 1.80, $t(113)=-5.01$, $p<.01$) surround effects were smaller. A repeated measures ANOVA indicates that there was an effect of surround configuration, $F(2, 226)=15.15$, $p<.01$. A Tukey contrast indicated that these effects were all significantly different from each other except for the collinear and full surround conditions (*p adjusted*=.28; *p adjusted*<.01 for all other comparisons).

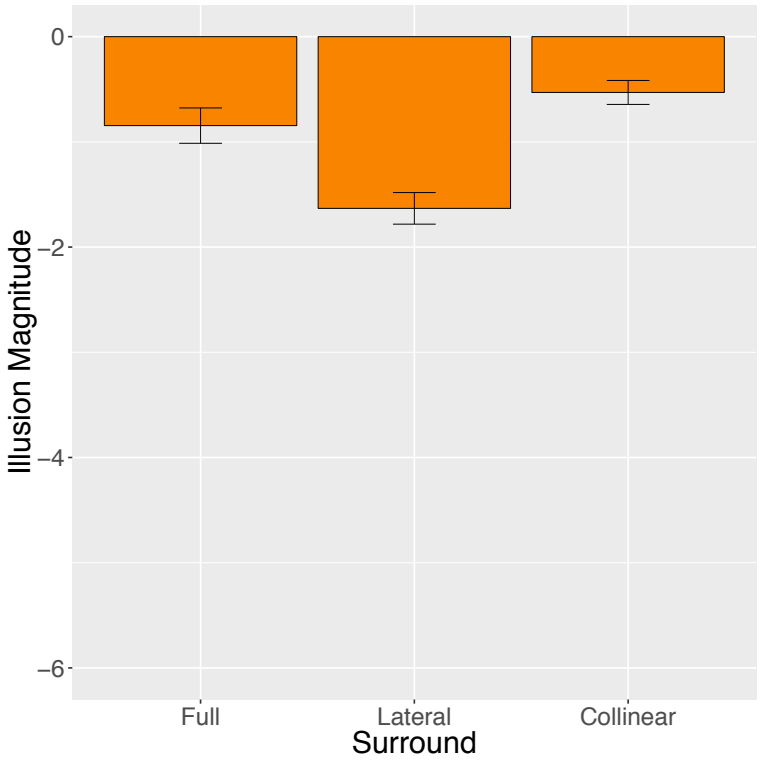

Figure 26. The mean shift in perception of the center under each surround configuration condition with a 75 degree surround tilt. Negative numbers indicate an attractive effect.

Next, we ran a linear model to determine the extent to which each regional surround condition predicts the effect of the full surround. We found that neither of the partial surround effects predicted the full surround effect (B_{col} = 0.19, B_{lat} = -0.11, r^2 = 0.02, $F(2,111) = 1.18$, p=.31).

We ran a Spearman correlation to determine the relationship between orientation sensitivity and each effect (Figure 27). There was no significant correlation between sensitivity and the attractive effects of the full surround ($r(112)$=-0.11, p=.26), the collinear surround ($r(112)$=0.04, p=.65), or the lateral surround ($r(112)$=0.10, p=.29). These results were the same even when we removed outlier subjects.

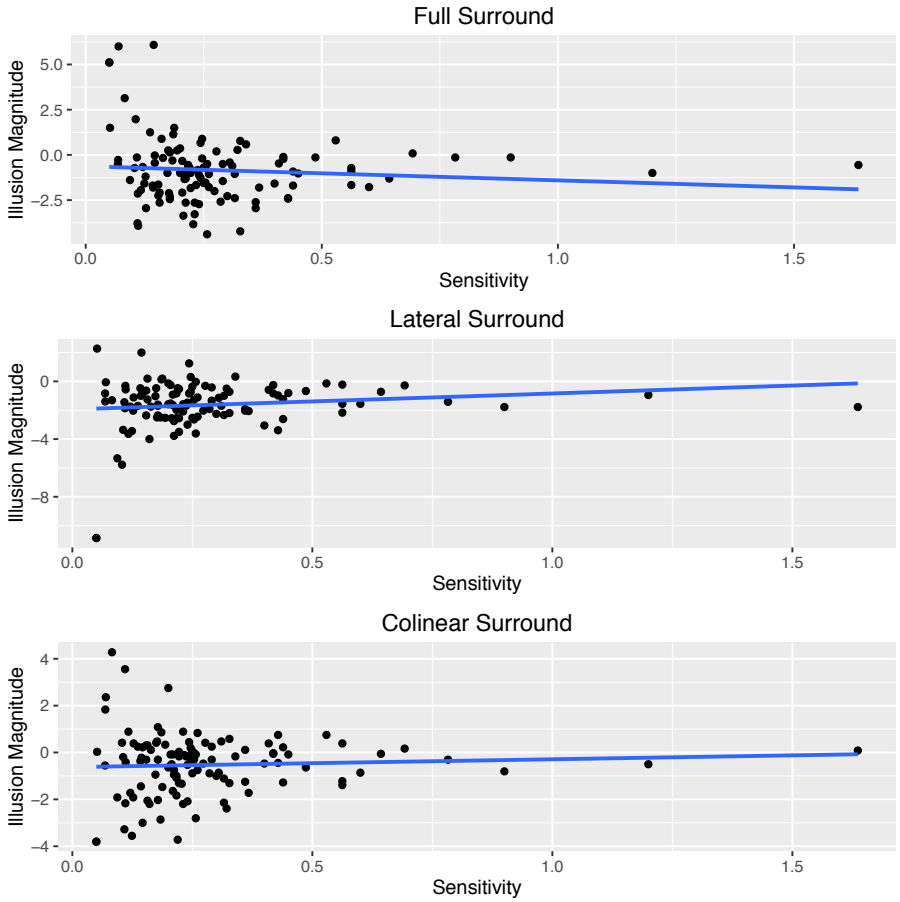

Figure 27. The relationship between orientation sensitivity and attractive surround effects.

Discussion

Regional contributions to the full surround effect

In this study we tested the extent to which the collinear and lateral regions of the full surround STI stimulus contribute to the overall surround effect. Based on the predictions of a divisive normalization model tuned to natural scene statistics, we hypothesized that the collinear region would drive the full surround effect. In Experiment 1, all 15-degree surround configurations led to a repulsive tilt illusion. The full surround had the largest effect. The effect of the collinear region was larger than the effect of the lateral region. While both the lateral and collinear regional effects contributed to the full surround effect, this contribution was a weighted sum.

The effect of the collinear region was a greater predictor of the magnitude of the full surround effect. The collinear region appears to be driving the effect of the full surround in two ways. First, the effect of the collinear region is larger. Because the collinear region is more likely than other regions to be co-assigned to the same object as the center it will have a larger normalizing impact on the center. Second, the effect of the collinear region is a stronger predictor of the effect of the full surround. This indicates that the impact of multiple regions is the sum of the regional effects weighted by the probability of their dependency on the center.

Based on Coen-Cagli et al's (2012) model, we predicted that the collinear region, having a higher probability of co-assignment with the center, would normalize the center and lead to the largest attractive effect. In Experiment 2, all 75-degree surround configurations led to small, but significant, attractive effects. However, unlike the effects of the 15-degree surround, the largest 75-degree surround effect (i.e. the most attractive effect) was from the lateral surround region. Although these findings are counter to what we predicted, they are not totally unreasonable given that the attractive effect is predicted to occur when the surround weakly activates the center but still has some probability of co-assignment. It is possible that the large, high contrast 75-degree surrounds are too strong of an input to maximize the attractive effect. If this were the case, then regions that have a high probability of co-assignment (i.e. collinear regions) would have too much suppressive input to observe a strong attractive effect. However, where that normalization was weaker (i.e. the lateral regions) there may be the

right balance of input strength and probability of co-assignment to observe the largest attractive effect.

The attractive effect has been well documented with the 75-degree full surround (Clifford, 2014; Westheimer, 1990). However, the full surround effect actually is somewhat smaller than the effect of the lateral region alone. This may be because the full surround is the weighted sum of the lateral and collinear regions. Although the weak normalization of the lateral regions leads to a larger attractive effect, it also makes for a weak contributor to the full surround.

Together, the results from these experiments indicate that the prior probability of dependency interacts with the strength of the stimulus input. The largest repulsive effect happens when strong stimulation normalizes the center response. The largest attractive effect happens when the stimulus input strength and prior probability of co-assignment are weak. The overall effect is a sum of the regional effects weighted by their dependency to the center. These results are consistent with a system that uses prior experience with natural scene statistics to integrate regions of space. This Bayesian estimate of the response distribution may be an efficient way for the visual system to represent information (Schwartz et al., 2006).

Regional Connectivity

We also addressed potential differences in the regional integration mechanisms by measuring the relationship between effect size and orientation sensitivity, which we use as an indicator of horizontal connectivity (Song et al., 2013; 2013b). As predicted, we observed a negative correlation between the full 15-

degree surround effect size and sensitivity. Although this relationship was not as strong as predicted, it is consistent with the results from Song et al. (2013) and may indicate that individual differences in the magnitude of the full surround effect are related to differing amounts of horizontal connectivity. We did not see this correlation with the full 75-degree surround. This could indicate that the 75-degree surround effect is not as dependent on the limitations of horizontal connectivity, or possibly that the attractive effects rely more on different types of connections, such as feedback or local connections associated with disinhibiton. Although we cannot directly determine this from our study, some researchers have suggested that the attractive effects stem from feedback while repulsive effects stem from horizontal connections (Smith and Wenderoth, 1999; Wenderoth & Johnstone, 1988). However, it has been determined that both surround suppression and facilitation rely on both feedback and horizontal inputs (Kim and Freeman, 2014). Therefore, the lack of correlation between the 75-degree surround effect and orientation sensitivity could indicate less reliance on horizontal connections, but are unlikely to indicate a complete absence of reliance.

We had expected that the collinear surround would be the surround configuration whose effect would be most correlated with sensitivity, which would indicate that the collinear region relied more on horizontal connections. Previous research has show that there are increased synapses associated with inputs from collinear regions compared to inputs from lateral regions (Lacaruso et al., 2017). However, we found that the relationship between sensitivity and the effect of the collinear region was not as strong or stable as the relationship between sensitivity

and the effect of the lateral surround region. It could be that as the visual system learns the statistics of the natural world the dependencies are accounted for with increases in neural connectivity. For example, prior experience with natural scenes may lead to increased horizontal connectivity between regions that are more likely to be part of the same object. However, it is also possible that the prior probability of dependency is predicted by higher-level areas and shared with V1 through feedback mechanisms. In this case, feedback would selectively enhance the normalizing effect of the collinear regions. Both lateral and collinear regions seem to be at least somewhat dependent on horizontal connectivity so we could think of the feedback as a way to gate the horizontal effects using prior expectations. This could explain why our results indicate that the effect of the collinear regions is not as limited by horizontal connectivity and why the effect of the collinear region is larger than the effect of the lateral region.

Another possibility is that the effects of the lateral region are simply more sensitive to the limitation of horizontal connectivity. The weaker dependency may mean that subtle changes in connectivity are related to more observable changes in effect size. However, if this were the case then we would expect that we would see a stronger relationship between orientation sensitivity and surround effects that occur with weak dependency (i.e. attractive effects). This could be especially true for the lateral attractive effects. The attractive effects need a balance of weak stimulation from neurons that respond to orientations that have a large difference from the orientations that are preferred by the neurons that respond to the center stimulus. The effect's reliance on input from larger distances in orientation-mapped

space could make it sensitive to the physical limitations of horizontal connections. However, that is not what we see. Therefore, it seems that the best explanation would be that the collinear repulsive effects rely on horizontal input as well as feedback from higher areas to provide additional information about dependency.

However, more work is needed before drawing these conclusions. Future studies could address the relative contributions of different components of surround effects. If the effect of the collinear region is driven by a combination of horizontal and feedback connections, we would expect its effect to have a different time course than the effects of the lateral regions. Another possibility is that the effect of the collinear region that is driven by feedback may be more resistant to a gap between the center and surround. Finally, we could also predict that the effect of the collinear region would be impacted by top-down effects, such as attention.

Conclusions

The 15-degree full surround leads to the largest repulsive effect and is a weighted sum of the lateral and collinear regional effects. The 75-degree lateral surround leads to the largest attractive effect but has little influence on the full surround attractive effect. The overall surround effect is a sum of the regional effects weighted by their dependency to the center. These results are consistent with predictions about a system that uses prior experience with natural scene statistics to integrate regions of space. Predictive signals based on the dependencies in natural scene statistics may feedback into V1 to selectively influence the effect of the horizontal signals on the tilt illusion.

CHAPTER 3: TO WHAT EXTENT DO AUTISTIC TRAITS PREDICT REGIONAL SURROUND INTEGRATION EFFECTS?

In our second study, we determine the extent to which autistic traits are associated with changes in orientation sensitivity and spatial integration. This has potential implications for understanding changes to integration mechanisms in disorders that have disrupted perception.

Background

The STI is a well-established paradigm for studying spatial integration (Clifford, 2014; Gibson & Radner, 1937; Westheimer, 1990). Here, the surrounding stimulus biases the perceived orientation of a simultaneously presented central test stimulus. The magnitude of the bias depends on the angular difference between the orientations of the inducing and test stimuli. Specifically, strong repulsive effects are observed when the difference between the angle of the center and surround is 10-20 degrees. The attractive effect is much smaller than the repulsive effect and is maximally observed when there is a relative difference of 75-80 degrees.

There is a relationship between the magnitude of the repulsive effect and orientation sensitivity. Individuals who are more sensitive to orientation changes are less susceptible to the influence of a 15-degree repulsive surround (Song et al., 2013). This relationship is thought to be a result of individual differences in cortical surface area. Specifically, a person would be more sensitive to changes in a large representation of a stimulus, where more neurons are recruited to encode the stimulus. Increased cortical surface area would also reduce the relative reach of intracortical connections, which may not be able to scale with cortical size. This

reduction in horizontal connections could lead to a reduction in surround suppression. In fact, Song et al. (2013) found that both orientation discrimination threshold and the magnitude of the contextual effect are negatively correlated with V1 surface area (but not V2 or V3) as measured by phase-encoded retinotopic mapping in fMRI.

Song et al. (2013) simulated the relationship they found between sensitivity and context effects by varying horizontal connectivity with cortical size. This simulation showed that horizontal connectivity within V1 may explain the relationship between individual differences in surround effects and orientation sensitivity. This is supported by fMRI studies showing that intrahemispheric connectivity in V1 is correlated with the magnitude of the tilt illusion (Song et al., 2013b; Song & Rees, 2018) and that cortical surface area is correlated with orientation sensitivity (Song et al., 2015). Together these results indicate that the relationship between orientation sensitivity and the magnitude of the tilt illusion is related to individual differences in horizontal connectivity.

There is also evidence that horizontal connectivity between the center and surround may vary with surround regions. There is more connectivity between receptive fields that are co-axially aligned and co-oriented to the center receptive field, and the number of connections between co-axially aligned receptive fields decreased as the orientation deviated from the orientation preference of the center receptive field (Lacaruso et al., 2017). Laterally aligned receptive fields had fewer connections to the center receptive field and the number of connections did not depend on orientation preference. This demonstrates increased connectivity

between receptive fields representing regions of space that have a higher probability of being co-oriented and, therefore, part of the same edge.

The relationship between the magnitude of the context effects and orientation sensitivity may be connected to a process that is affected in autism. There is evidence that people with autism are less susceptible to the influence of contextual stimuli (Happe & Firth, 2006) and have a local processing bias (Dakin & Frith, 2005).

These differences may be related to alterations in a delicate excitatory-to-inhibitory response balance. It has been proposed that an elevated ratio of excitatory to inhibitory responses could explain to some of the social and perceptual impairments seen in autism (Rubenstein & Merzenich, 2003). It is important to note that there are several factors that could lead to an altered balance of excitatory and inhibitory responses in autism (see Nelson & Valakh, 2015). A reduction in surround suppression and an elevated excitatory-to-inhibitory response ratio in autism can be modeled with divisive normalization (Rosenberg, Patterson, & Angelaki, 2015). Rosenberg et al. (2015) determined the activity of a population of model neurons using a normalization function. In this function, the gain term determines the neuron's sensitivity to the context information. It scales the suppressive field input so that a small gain term will lead to less suppression. To model autism, the authors reduced the gain term by 25%. They found that this reduction in the gain term led to a reduction in surround suppression for visual context stimuli in the "ASD" (autism spectrum disorder) model neurons. Rosenberg et al. (2015) set the gain term as a constant but it could also be a function of tuning

properties with experience (Schwartz & Coen-Cagli, 2013). That is, prior experience with natural scenes will tune responses as a way to optimize neural coding. Therefore, it is possible that people with autism do not rely on prior experience as much as the typically developing population.

In fact, a recent study shows that the simple divisive normalization model used in Rosenberg et al. (2015) cannot explain the intact perceptual bias found in a group of participants with autism (Van de Cruys, Vanmarcke, Steyaert, Wagemans, 2018). They found that there was no difference between tilt illusions in participants diagnosed with ASD and neurotypical controls for a cross orientation suppression task. The authors argue that this is clear evidence against a decreased divisive normalization model of ASD in low-level perception. However, they do not rule out the possibility of a flexible normalization model as a way to predict when surround suppression will be reduced and when it will not be reduced for people who have autism (or score high on autistic traits). We could imagine that a flexible model that is tuned to natural scene statistics would predict that surround suppression is reduced in people with autism only when the target and inducer are perceived to be part of the same object. In this case these two studies may be in some agreement about the possible change in (e.g., reduction or slower processing) reliance on priors for ASD participants, despite Van de Cruys et al. (2018) opposition to Rosenberg et al's. (2015) use of the normalization model.

There are often complications associated with testing an ASD population and finding well-matched controls. Another option is to search for correlations between perceptual biases and various autistic traits. Autistic traits have been found to exist

as a continuum in the general population, with individuals on the autistic spectrum tending to score at the extreme ends of the continua (Baron-Cohen, Wheelwright, Skinner, Martin & Clubley, 2001; Wheelwright et al., 2006). These traits are measured with the empathizing quotient (EQ, a measure of drive to recognize and respond to other's emotional state; Baron-Cohen & Wheelwright, 2004), the systemizing quotient (SQ, a measure of the drive to analyze, understand, predict, control and construct rule-based systems; Baron-Cohen, Richler, Bisarya, Gurunathan, & Wheelwright, 2003), and the Autism Quotient (AQ, which is a broadband measure of individual differences in traits related to Autism; Baron-Cohen, Wheelwright, Skinner, Martin & Clubley, 2001). People with autism tend to have high SQ and AQ scores and low EQ scores.

There is evidence that people who score high on AQ show decreased surround suppression (Flevaris & Murray, 2015) and increased orientation sensitivity (Dickinson, Jones & Milne, 2014; although also see Shafai, Armstrong, Iarocci & Oruc, 2015 for evidence that there is no enhancement in orientation processing for individuals with ASD).

What is currently unknown is the extent to which autistic traits will predict changes to suppression and facilitation from different surround regions. If the autistic traits are representative of a reduction in reliance on prior experience with natural scenes then we would predict that the probability of co-assignment of the center and surround would be similar for collinear and lateral surround regions. This would be brought about by a reduction in the collinear surround effect only, causing it to become more similar to the lateral surround effect. Therefore, we

would expect a smaller difference between the regional effects for people who score high on autistic traits. Alternatively, if the autistic traits were representative of a general reduction in reliance on prior experience then we would predict that the difference between the effects would be the same but the overall effects would be smaller for people who score high on autistic traits.

It is also unknown the extent to which individual differences in the magnitudes of autistic traits can account for the relationship between sensitivity and effect size. If the relationship between sensitivity and context effects for people who score high on AQ is due to a lower level of horizontal connectivity then we would predict that AQ would fully account for the relationship between sensitivity and context effects. However, if the relationship between sensitivity and context effects for people who score high on AQ were unrelated to horizontal connectivity then we would predict that AQ would uniquely contribute to the variance of the effect.

We hypothesize that people who score high on AQ will show reduced surround effects for all surround types. We also hypothesize that AQ score will not fully account for the relationship between sensitivity and the magnitude of the surround effect.

Methods

To determine the effects of individual differences in autistic traits on regional surround effects and sensitivity, we included measures of autistic traits in Experiment 1 (surrounds rotated 15 degrees) and Experiment 2 (surrounds rotated 75 degrees) from Chapter 2.

We determined the illusory effect of the full STI and compared it to the effect driven by surrounding contexts limited to isolated collinear and lateral regions, with orientation sensitivity additionally measured with no surround. These effects were measured using a two alternative forced choice task, which was created using PsychoPy2 Experiment Builder (v1.84.2; Peirce, 2009).

The experiment took place in a small darkened room with walls painted black. All stimuli were presented on a 27" Apple Mac Pro with resolution of 2560 x 1440 pixels. A black circular mask was placed over the monitor so that the edges of the monitor could not be used as orientation references.

Participants

225 participants (110 in Experiment 1 and 115 in Experiment 2) volunteered in exchange for course credit or for a payment of $10.

Stimuli

In Experiment 1, the surrounds were oriented either 15 degrees CW or CCW from the reference orientation (45 degrees). On average, this tilt leads to perceptual repulsion for the full surround conditions. In Experiment 2, the surrounds were oriented either 75 degrees CW or CCW from the reference orientation. On average, this tilt leads to perceptual attraction for the full surround conditions. There were 7 conditions in each experiment: 3 surround shapes (full, lateral, or collinear) x 2 surround orientations (Exp. 1: 15 degrees CW or CCW; Exp. 2: 75 degrees CW or CCW) + no surround (1). See Chapter 2 for details about the stimuli.

Procedure

On each trial, participants were presented with a sequential set of stimuli: a reference and a probe. The reference was always a 45-degree center stimulus with no surround. The probe was a center stimulus that was either alone or accompanied by a surround depending on the condition. The probe configuration was pseudo-randomly chosen from the seven stimulus conditions described above. The orientation of the probe was determined using a staircasing procedure. See Chapter 2 for details about the procedure.

After participants completed the experimental task, they completed the AQ and SQ-R, which are self-report questionnaires of 60 and 75 questions, respectively (Baron-Cohen et al., 2001; Wheelwright et al., 2006). Each questionnaire consists of a set of statements in which responses are measured on a 4-point Likert scale (definitely agree, slightly agree, slightly disagree, definitely disagree). We also extracted values from two subscales of the SQ: Insistence on Sameness (IS) and Analytical Tendencies (AT, Reed & Dassonville, in progress). IS was determined by summing SQ-R items 2, 14, 20, 21, 28, 31, 44, 55, 56, 65, 71 and 72. AT was determined by summing SQ-R items 6, 7, 8, 9, 10, 11, 15, 16, 17, 18, 25, 26, 27, 30, 32, 34, 35, 40, 41, 45, 46, 50, 53, 60, 70 and 74.

There is some evidence that there is a relationship between the SQ subscales and context effects. Scoring high on IS is associated with increased local contrast effects while scoring high on AT is associated with increased global contrast effects (Reed & Dassonville, in progress). It is possible that we may see a correlation with IS and the magnitude of the STI, given that it is thought that the tilt illusion arises from local contrast effects.

Analysis

We determined the effect of each surround by averaging the effects of the CW and CCW versions of each surround configuration for each subject. We calculated sensitivity as the inverse of the sensitivity threshold (difference between 45 degrees and the degree at which participants reported the probe being CW 70.7% of the time). See Chapter 2 for more details about this analysis. One participant was removed from Experiment 1 and one participant was removed from Experiment 2 because we were unable to compute their orientation sensitivity when the staircases failed to converge.

Results

Experiment 1 (15 degree surround)

For each subject, we calculated their AQ, SQ-R, IS, and AT scores. The summary of these scores is shown in Table 1. The AQ and SQ-R values we measured were similar to the median scores in the population (Baron-Cohen et al., 2001; Wheelwright et al., 2006). The AQ values we measured were also similar to the values found by Flevaris and Murray (2015; AQ scores ranged from 9 to 34, and the median score was 19.)

	AQ	**SQ-R**	**IS**	**AT**
N	101	101	101	101
Range	8 - 40	21 - 117	2 - 24	3 - 38
Median	19	60	11	21

Table 1. Descriptive statistics for autistic trait measures.

We performed a median split on the autistic traits and report the mean effect size for the surround configurations and sensitivity in Table 2.

	AQ		SQ-R		SQ-R: IS		SQ-R: AT		Overall
	Hi	*Lo*	*Hi*	*Lo*	*Hi*	*Lo*	*Hi*	*Lo*	
Sensitivity	0.33 (0.25)	0.28 (0.16)	0.33 (0.24)	0.27 (0.18)	0.28 (0.17)	0.33 (0.25)	0.34 (0.25)	0.26 (0.13)	0.30 (0.20)
Full Surround	5.94 (1.39)	6.13 (1.67)	5.86 (1.36)	6.32 (1.58)	6.29 (1.53)	5.93 (1.47)	5.87 (1.28)	6.29 (1.56)	6.03 (1.52)
Lateral Surround	3.54 (1.23)	3.83 (1.43)	3.54 (1.10)	3.94 (1.49)	3.84 (1.45)	3.62 (1.28)	3.55 (1.18)	3.90 (1.33)	3.74 (1.29)
Collinear Surround	4.59 (1.52)	4.83 (1.46)	4.62 (1.36)	4.85 (1.40)	4.91 (1.42)	4.69 (1.49)	4.69 (1.31)	4.79 (1.38)	4.76 (1.43)

Table 2. The mean effect sizes for sensitivity and 15 degree surrounds when participants are grouped as scoring either high or low on the personality traits. Standard deviation is in parentheses.

First we determined if there was a relationship between autistic traits and sensitivity. We correlated participants' score on each trait with their orientation sensitivity using a Spearman correlation. None of the correlations were significant. Next, we compared orientation sensitivity for subjects who scored "high" or "low" on each trait based on a median split (Figure 28). This method was used by Flevaris and Murray (2015) in their analysis. Using a one tailed t-test we found a non-significant trend that people who scored high on AQ were more sensitive to changes in orientation ($t(75.85)= 1.00$, $p=0.16$). A similar possible trend was observed for SQ-R. Participants who scored high on SQ-R were more sensitive to changes in orientation ($t(89.95)= 1.46$, $p=0.07$). We did not have a specific prediction about the relationship between the SQ-R subscales and sensitivity so we examined them with a two-tailed test. Neither traits showed significant differences in sensitivity for participants who scored high or low. However, there was a trend that people who scored high on AT are more sensitive to orientation ($t(66.55)= 1.83$, $p=0.07$). Interestingly, although there was no significant difference between sensitivity for participants who scored high and low on IS, the average sensitivity for people who scored high on IS is smaller than for people who score low on IS ($t(71.44)= -1.07$, $p=0.29$). This is in the opposite direction of the trend with AT.

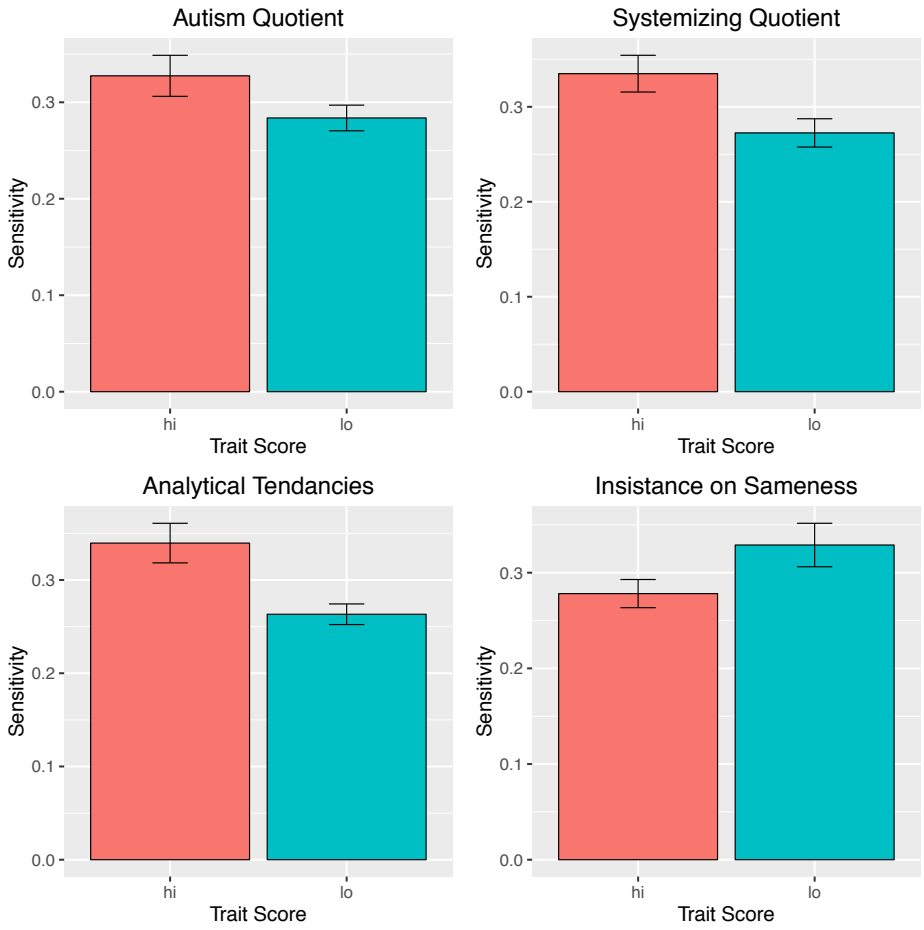

Figure 28. Orientation sensitivity grouped by score on autistic traits. Standard error is indicated with error bars.

Next, we determined if there was a relationship between autistic traits and surround effect sizes. We correlated participants' score on each trait with the effect of each surround configuration using Spearman correlations. None of the correlations were significant. Then we compared the magnitude of the surround effects for subjects who scored "high" or "low" on each trait based on a median split (Figure 29). We used a mixed effects model with trait as a between subject effect and surround region as a within subject effect (subject was a random effect). There was a main effect of surround region ($F(2,184)=144.84$, $p<.01$). The full surround yielded the largest effect followed by the collinear surround and then the lateral

surround (more details about these effects are available in Chapter 2). There was no significant effect of AQ ($F(1,92)=0.88$, $p=0.35$) and no interaction ($F(2,184)=0.06$, $p=0.94$). There was also no significant effect of SQ-R ($F(1,94)=2.30$, $p=0.13$) and no interaction ($F(2,188)=0.40$, $p=0.67$). There were also no significant main effects of the SQ-R subscales (IS: $F(1,87)=1.05$, $p=0.31$; AT: $F(1,91)=1.47$, $p=0.23$) and no significant interactions between subscales and surrounds (IS: $F(2,174)=0.16$, $p=0.86$; AT: $F(2,182)=0.86$, $p=0.43$). Although none of these effects were significant, the means were trending in the direction as predicted: people who score high on AQ and SQ show overall lower effects of the surround. Mean surround effects were lower for participants who scored high on AT, but higher for participants who scored high on IS.

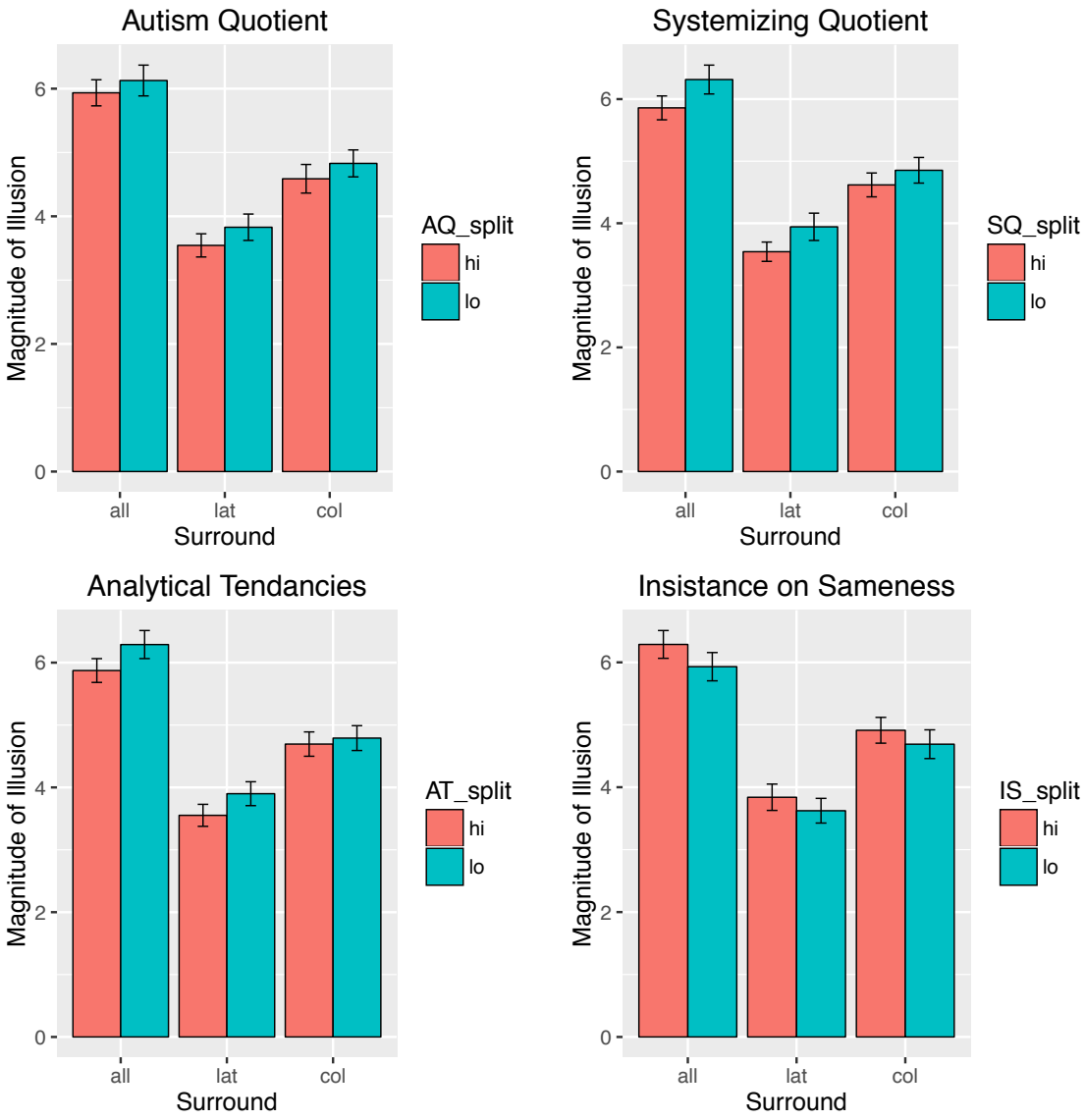

Figure 29. Effect of each surround on perception of central stimulus grouped by score on autistic traits.

We had planned on running a mediation analysis to determine if autistic traits could predict regional effects above and beyond what is predicted by orientation sensitivity. However, since there were no correlations between autistic traits and the effects of the surrounds it would not be meaningful to conduct the analysis.

Experiment 2 (75 degree surround)

For each subject, we calculated their AQ, SQ-R, IS, and AT scores. The summary of these scores is shown in Table 3. The AQ and SQ-R values we measured are similar to the median scores in the population and previous studies (Baron-Cohen et al., 2001; Flevaris & Murray, 2015; Wheelwright et al., 2006).

	AQ	**SQ-R**	**IS**	**AT**
N	90	100	100	100
Range	6 - 32	19 - 118	1 - 23	1 - 43
Median	17	60.5	13	20

Table 3. Descriptive statistics for autistic trait measures.

We performed a median split on the autistic traits and report the mean effect size for the surround configurations and sensitivity in Table 4.

	AQ		SQ-R		SQ-R: IS		SQ-R: AT		Overall
	Hi	*Lo*	*Hi*	*Lo*	*Hi*	*Lo*	*Hi*	*Lo*	
Sensitivity	0.27 (0.18)	0.30 (0.28)	0.30 (0.22)	0.28 (0.23)	0.29 (0.25)	0.30 (0.20)	0.33 (0.22)	0.26 (0.23)	0.28 (0.22)
Full Surround	-1.17 (1.39)	-0.55 (2.21)	-0.80 (1.50)	-1.05 (2.00)	-1.01 (1.45)	-0.95 (1.94)	-0.97 (1.27)	-0.80 (2.15)	-0.85 (1.80)
Lateral Surround	-1.59 (1.08)	-1.60 (1.99)	-1.69 (1.69)	-1.39 (1.11)	-1.92 (1.72)	-1.22 (1.08)	-1.49 (1.06)	-1.57 (1.78)	-1.63 (1.76)
Collinear Surround	-0.55 (1.34)	-0.40 (1.37)	-0.66 (1.13)	-0.34 (1.42)	-0.58 (1.13)	-0.40 (1.42)	-0.59 (1.04)	-0.43 (1.53)	-0.53 (1.34)

Table 4. The mean effect sizes for sensitivity and 75 degree surrounds when participants are grouped as scoring either high or low on the personality traits. Standard deviations are in parentheses.

First we determined if there was a relationship between autistic traits and sensitivity. We correlated participants' score on each trait with their orientation sensitivity using a Spearman correlation. None of the correlations were significant. Next, we compared orientation sensitivity for subjects who scored "high" or "low" on each trait based on a median split (Figure 30). Using a one tailed t-test we found that there was no significant difference between sensitivity for participants who score high and low on AQ ($t(65.04)= -0.61$, $p=0.73$). A similar null result was observed for SQ-R ($t(97.75)= 0.46$, $p=0.33$). We did not have a specific prediction about the relationship between the SQ-R subscales and sensitivity so we examined them each with a two-tailed test. Neither traits show significant differences in sensitivity for participants who score high or low (IS: $t(84.71)= -0.22$, $p=0.82$; AT: $t(90.46)= 1.37$, $p=0.17$).

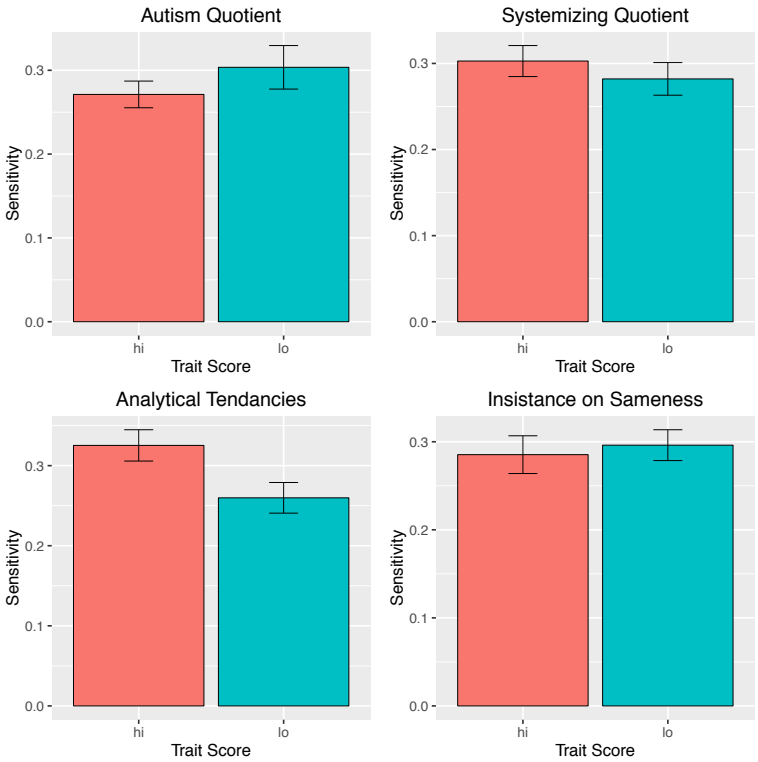

Figure 30. Orientation sensitivity grouped by score on autistic traits.

Next, we determined if there was a relationship between autistic traits and surround effect sizes. We compared the magnitude of the surround effects for subjects who scored "high" or "low" on each trait based on a median split (Figure 31). We used a mixed effects model with trait as a between subject effect and surround orientation as a within subject effect (subject was a random effect). There was a main effect of surround ($F(160)=11.62$, $p<.01$). The lateral surround yielded the largest effect followed by the collinear surround and then the full surround (more details about these effects are available in Chapter 2). There was no significant effect of AQ ($F(1,80)=1.22$, $p=0.27$) and no interaction ($F(2,160)=0.95$, $p=0.39$). There was also no significant effect of SQ-R ($F(1,98)=0.36$, $p=0.56$) and no interaction ($F(2,196)=1.41$, $p=0.25$). There were also no significant main effects of the SQ-R subscales (IS: $F(1,87)=2.32$, $p=0.13$; AT: $F(1,91)=0.14$, $p=0.70$) and no significant interactions between subscales and surrounds (IS: $F(2,174)=1.34$, $p=0.26$; AT: $F(2,182)=0.24$, $p=0.79$). When we split participants into three groups and compare the extreme groups we find a significant main effect of IS ($mean_{high} = -1.32$, $mean_{low} = -0.57$, $F(1,57)=8.85$, $p<.01$). All other comparisons using the three-way split were non-significant.

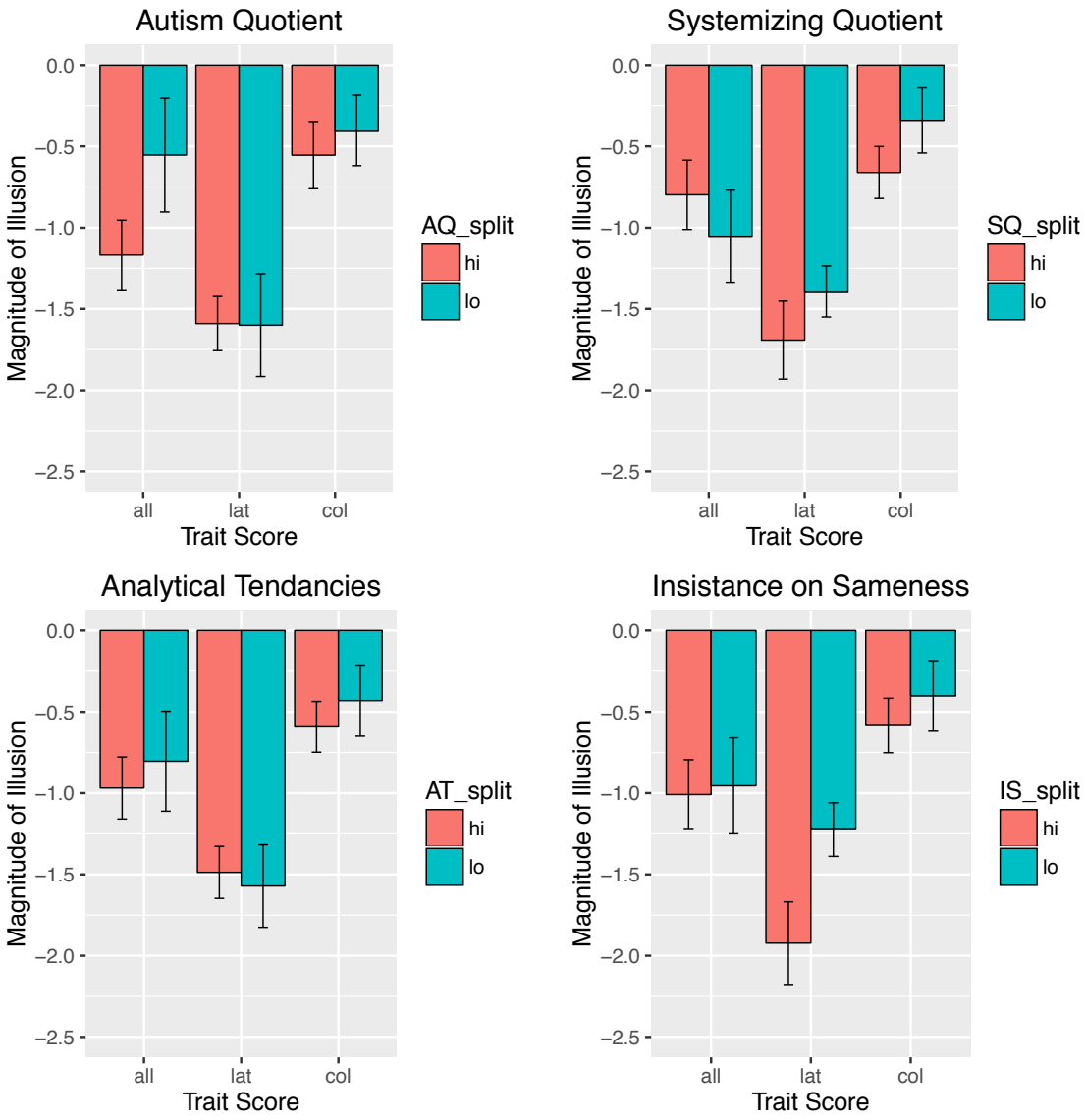

Figure 31. Effect of each surround on perception of central stimulus grouped by score on autistic traits.

Next, we correlated participants' score on each trait with their effect if each surround configuration using Spearman correlations. We observed a negative correlation between IS and the 75 degree lateral surround effect ($r(112)$=-0.25, p=.01, Figure 32). Although we observed a main effect of IS for the three-way split of the trait data, there was no correlation with the collinear surround effect

($r(112)$=-0.13, p=.20), or the full surround effect ($r(112)$=-0.07, p=.50). None of the other correlations were significant.

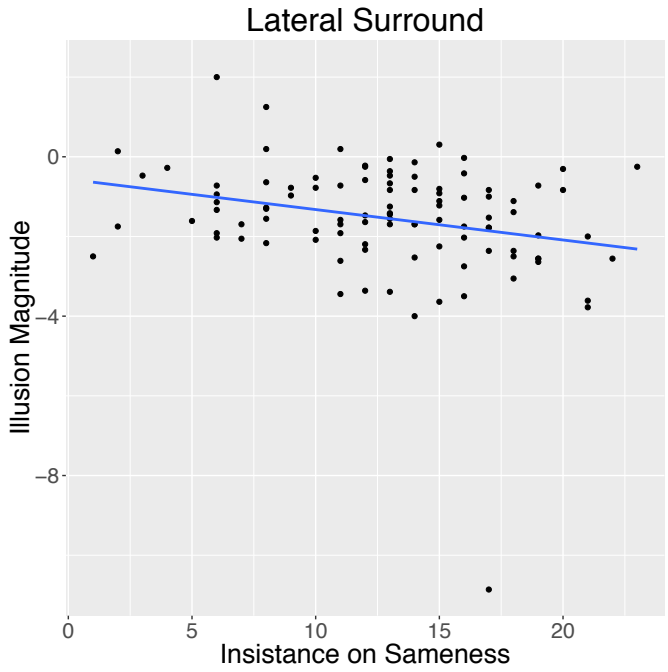

Figure 32. Relationship between Insistence on Sameness score and the effect of the 75-degree lateral surround.

We had planned on running a mediation analysis to determine if autistic traits could predict regional effects above and beyond what is predicted by orientation sensitivity. The most promising mediation would be to estimate the effect of sensitivity on the effect of the 75-degree lateral surround as mediated by IS. There is a correlation between the effect of the 75-degree lateral surround and IS score. However, there was no correlation between sensitivity and IS or between the effect of the 75-degree lateral surround and sensitivity. Therefore, it is not meaningful to run a mediation analysis.

Combined Sensitivity Data

We decided to combine the orientation sensitivity data from Experiment 1 and 2. Orientation sensitivity was calculated using trials from the no-surround condition. This condition was identical in both experiments and pooling them gave us data from 223 participants (140 female, 77 male, 6 undisclosed). This would allow us to substantially boost power so that we could identify very small effects and reduce our probability of Type II error.

We correlated participants' score on each trait with their orientation sensitivity using a Spearman correlation. None of the correlations were significant. Next, we compared orientation sensitivity for subjects who scored "high" or "low" on each trait based on a median split (Figure 33). Using a one tailed t-test we found that there was no significant difference between sensitivity for participants who score high and low on AQ ($t(160.92)= 0.75$, $p=0.77$). A similar null result was observed for SQ-R ($t(177.28)= 0.97$, $p=0.17$). We did not have a specific prediction about the relationship between the SQ-R subscales and sensitivity so we examined them each with a two-tailed test. There was no significant difference in sensitivity for participants who score high or low on IS ($t(183)= -0.70$, $p=0.48$). However, participants who scored high on AT had significantly higher orientation sensitivity ($t(183)= 2.24$, $p=0.03$).

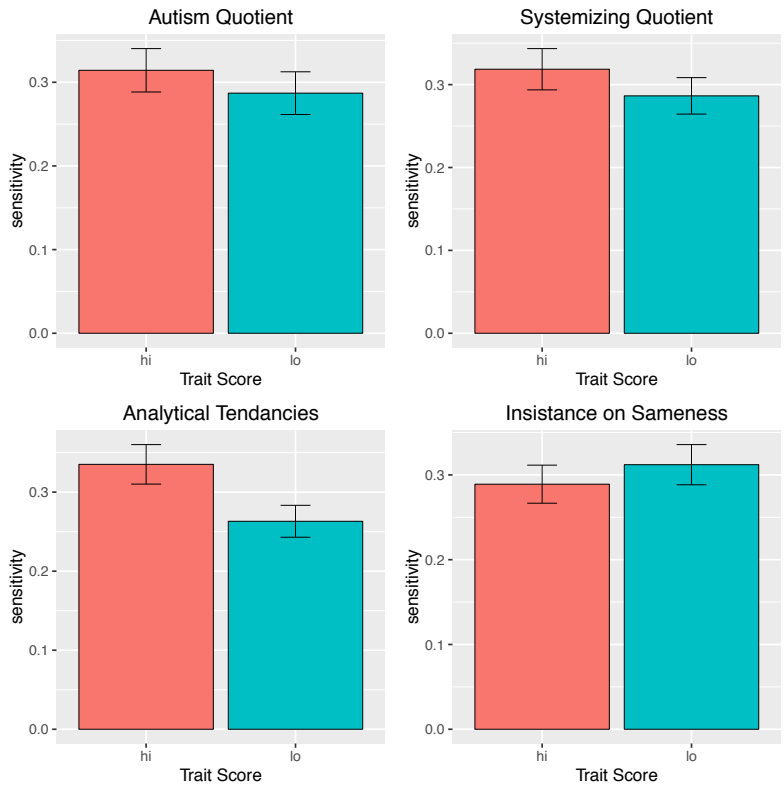

Figure 33. Orientation sensitivity grouped by score on autistic traits for data pooled between Experiment 1 and Experiment 2.

Our data also show that males have higher orientation sensitivity than females ($t(129.1)=2.41$, $p=.02$; Figure 34). Modeling sensitivity as a function of sex and AT score significantly accounts for more variance than AT alone ($F(1,181)=4.44$, $p=.01$). In fact, the effect of AT becomes non-significant. This indicates that these effects may be linked to sex differences.

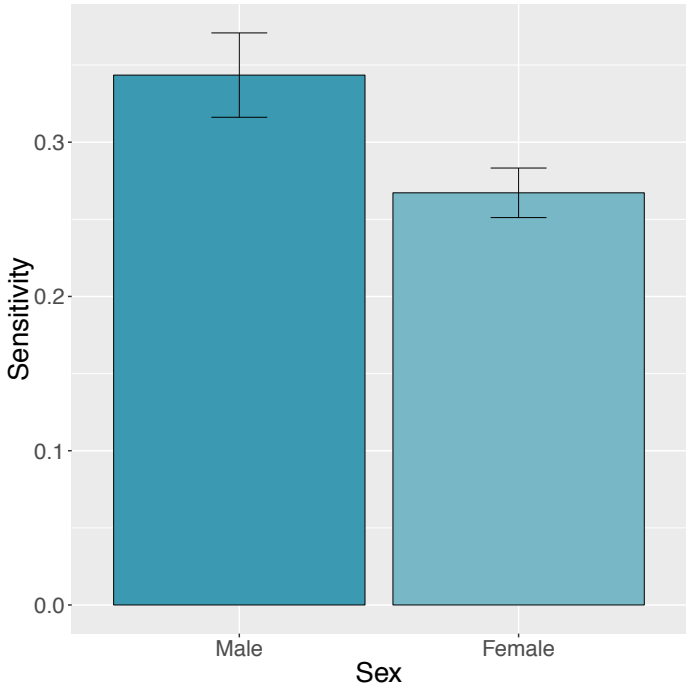

Figure 34. Orientation sensitivity grouped by sex for data pooled between Experiment 1 and Experiment 2.

Discussion

The purpose of the study was to determine the extent to which autistic traits predicted orientation sensitivity and regional surround effects. In both experiments we observed median AQ and SQ scores that are comparable to previous literature (Baron-Cohen et al., 2001; Flevaris & Murray, 2015; Wheelwright et al., 2006). There is evidence that people who score high on AQ show increased orientation sensitivity (Dickinson et al., 2014). Although there was no significant difference between orientation sensitivity for participants who scored high and low on autistic traits in Experiment 1 and 2, we found a significant effect of AT score when we pooled the participants from both studies. People who score high on AT had higher sensitivity than people who scored low on AT. However, it appears that this effect is actually driven by sex differences. We found that males have significantly higher orientation

sensitivity than females. This analysis also provides stronger evidence that AQ, SQ-R and IS are not related to orientation sensitivity. This finding is inconsistent with the findings of Dickinson et al., (2014). However, the inconsistent observation of this relationship is also evident in the previous literature (Shafai, Armstrong, Iarocci & Oruc, 2015).

We measured the extent to which the perceptual attractive and repulsive effects of the surrounds were predicted by autistic traits. There is evidence that people who score high on AQ show decreased surround suppression (Flevaris & Murray, 2015). However, we did not observe any decreases in perceptual repulsion related to any of the autistic traits. We did observe a reduction in the 75-degree lateral surround effect as IS score increased. The 75-degree lateral surround effect is the largest attractive effect of all of the surround configurations and has the least amount of suppressive input. Therefore, it is possible that IS is related to the attractive component of the surround effect. Previous work has demonstrated that IS score is related to local contrast effects (Reed & Dassonville, in progress). It may be that IS is related to individual differences in the local disinhibition that is thought to drive attractive tilt effects.

Because of the previously observed relationships between AQ and orientation sensitivity (Dickinson et al., 2014) and surround suppression (Flevaris & Murray, 2015) we considered if AQ score would account for the relationship between orientation sensitivity and surround effects. This does not appear to be the case. We found that different SQ-R subscale traits were associated with orientation sensitivity (AT) and the attractive surround effects (IS). This is evidence that there

is not a single underlying factor to relate autism traits, surround effects and orientation sensitivity.

It is thought that an elevated ratio of excitatory to inhibitory responses would lead to some of the perceptual impairments seen in autism (Rubenstein & Merzenich, 2003). This can be modeled with divisive normalization by reducing a gain term (Rosenberg, Patterson, & Angelaki, 2015). On the other hand, previous work (Van de Cruys et al., 2018) has found that there is no difference in the normalization process between typically developing participants and those diagnosed with autism. However, they stated that it still could be possible to see differences between the groups when describing the effects with a flexible normalization model that accounts for experience with natural scenes. If the autistic traits were representative of a reduction in reliance on prior experience with natural scenes then we would predict reduction in the collinear surround effect only. Our results suggest that autistic traits do not lead to a reduction in flexible normalization.

Van de Cruys et al. (2018) also proposed that people with autism may still rely on prior experience with natural scenes but that their use of the prior may be delayed. In fact, a meta-analysis showed that people with autism process global information more slowly that neurotypical controls (Van der Hallen, Evers, Brewaeys, Van den Noortgate & Wagemans, 2015). Therefore, we would expect that people with autism (or neurotypical participants who score high on autistic traits) would show a delayed effect of the collinear surround. This would be an excellent area to follow up with future studies.

Conclusion

In conclusion, we found no evidence for reduced normalization in people who score high on autistic traits. In fact, high scores on the SQ-R subscale IS is associated with larger attractive effects. Males had higher orientation sensitivity than females. Together these results indicate that the relationships between autistic traits, sensitivity and surround effects are not as robust and are more nuanced than previously established. There does not seem to be a single factor relating these individual differences.

CHAPTER 4: TO WHAT EXTENT DOES AROUSAL MODULATE SPATIAL INTEGRATION?

In this study we determine the extent to which spatial integration is modulated by natural fluctuations in internal arousal states. Here, we measured the amount of perceptual repulsion caused by an oriented surround for cases of low and moderate arousal, as indexed by pupil size.

There is evidence that the extent to which surround information influences perception of a central target is dependent on state differences within a subject. During attentive and alert brain states cortical gain increases and surround effects are reduced. An indicator of brain state or cortical gain in animals is activity level of the subject. It is known that visual responses increase with locomotion (Bennett, Arroyo & Hestrin, 2013; Niell & Stryker, 2010), and that arousal increases neural sensitivity (Reimer et al., 2014; McGinley et al., 2015). The neural enhancement observed during locomotion is driven by nicotinic inputs from the basal forebrain activating VIP+ neurons in mouse V1 (Fu et al., 2014). Basal forebrain cholinergic neurons are also associate with wakefulness (Lee, Hassani, Alonso & Jones, 2005).

Ayaz, Saleem, Scholvinck, and Carandini (2013) have shown that locomotion also affects spatial integration. The authors recorded neurons in the primary visual cortex from head fixed mice placed on a spherical treadmill. They found that there was strong surround suppression when the mice were stationary. However, surround suppression decreased during locomotion. Typically the neural response to a stimulus increases with stimulus size up to an optimal point. Larger stimuli extend beyond this driving field and impinge on a suppressive surrounding field. In

mice that were moving, though, neural responses did not drop off with an increase in stimulus size. This effect matches what would be predicted by a response gain change. When Ayaz et al. (2013) modeled the results with a simplified gain normalization model they found that locomotion caused the baseline activity level to increase as well as the Drive/Suppression ratio. In some neurons, that ratio increase was due to an increase in drive; in others, it was because of a decrease in suppression.

While the effects of arousal on visual processing is quite convincing in animal studies, it is less convincing in humans. Benjamin, Wailes-Newson, Ma-Wyatt, Baker, and Wade (2018) did not find a decrease in contrast detection threshold when human subjects were instructed to walk briskly during the task. In fact, brisk walking seemed to increase the contrast masking effects of an iso-oriented surround. However, Kim, Lokey and Ling (2017) demonstrate that reward-based arousal does increase contrast sensitivity. Furthermore, others have found that orientation sensitivity increased during low intensity exercise (Bullock, Elliott, Serences & Giesbrecht, 2017). Therefore, it is possible to observe the effects of arousal, but locomotion may not be the best indicator of arousal in humans.

Instead, natural fluctuations in arousal can be indexed with pupil diameter (Aston-Jones & Cohen, 2005). Pupil dilation has been used, in humans (Gilzenrat et al., 2010) and animals (McGinley et al., 2015; Reimer et al., 2014), as an indicator of arousal responses as well as cortical desynchronization and activity of the locus coeruleus–norepinephrine system. The human studies described above show increases in pupil size when conditions yield moderate arousal. However, in these

studies the authors attempted to control the arousal level whereas in the animal studies researchers recorded natural fluctuations in arousal. This may be an important distinction to consider when translating the results between animal models and humans.

It is currently unclear how alertness and arousal modulate orientation specific surround effects in animals, and the extent to which this occurs in humans. It is unknown the extent to which passive changes in alertness, as indexed by pupil diameter, predict surround effects and orientation sensitivity within a subject. If alertness enhances neural sensitivity then we would expect that orientation sensitivity would increase during times of higher alertness. Likewise, if alertness reduces the normalizing effect of the surround then we would expect that surround suppression would decrease during times of higher alertness. It is also important to consider that while the average effect of the 15-degree STI is repulsive, some participants may show an attractive effect. Therefore, we will also consider the shift in the direction of all effects. An overall reduction in surround effects (i.e. individual effects shift toward 0) at moderate arousal states would suggest that arousal reduces surround integration. However, a reduction in the repulsive effect and an increase in the attractive effect (i.e. individual effects shift to facilitation) at moderate arousal states would indicate that arousal biases the modulatory effect of the surround to enhance perception of the target.

We hypothesize that the magnitude of the illusion will be largest when the participant is in a state of low arousal (indicated by a small pupil) and smallest when the participant is in a state of moderate arousal (indicated by a large pupil).

We further predict that there will be an increase in orientation sensitivity when the participants are in a state of moderate arousal. We also hypothesize that surround suppression will be negatively correlated with sensitivity, as we saw in Chapter 2.

Methods

To test these hypotheses we compared the illusory effect of the full 15-degree STI during times of moderate and low alertness, as indexed by pupil diameter. Orientation sensitivity was measured with no surround. These effects were measured using a two alternative forced choice task.

The experiment took place in a small darkened room. All stimuli were presented on a 27" Apple Mac Pro with resolution of 2560 x 1440 pixels. Pupil diameter was record using a desktop mounted Eyelink 1000. The experiment was created using PsychoPy2 Experiment Builder (v1.84.2; Peirce, 2009) and communicated with the eye tracker using the ioHub package. Pupil diameter and gaze position was recorded throughout each trial.

Participants

Thirty-one participants volunteered in exchange for course credit or for a payment of $10. A power analysis revealed that we would only need a minimum of 14 subjects to see the correlation that Song et al. (2013) observed between the full surround effect and orientation sensitivity.

Stimuli

On each trial, participants were presented with a sequential set of stimuli: a reference and a probe. The reference was always a 45-degree center stimulus with

no surround. The probe was a center stimulus that was either alone or accompanied by a full surround, depending on the condition.

All stimuli were presented on a grey, 50% luminance background. The center was a 1.5 diameter dva oriented sinusoidal grating with a hard aperture. The full surround was a circular annulus reaching to a full diameter of 6 dva with a hard aperture (Figure 35). The spatial frequency of all stimuli was 3 cycles/dva. The surrounds were oriented either 15 degrees clockwise (CW) or counter-clockwise (CCW) from the reference orientation. On average, this orientation leads to perceptual repulsion. There were 3 conditions: surround orientation (2: 15 degrees CW or CCW) + no surround (1).

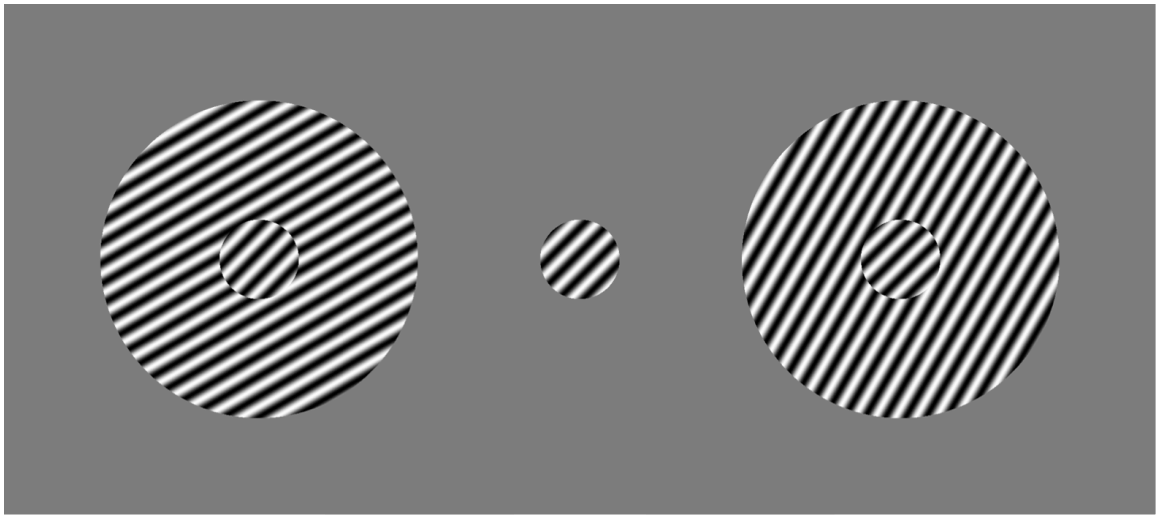

Figure 35. Stimuli with a 45 degree center and surrounds tilted 15 CW and CCW from the 45 degree reference.

Procedure

The presentation order of the probe and reference was randomized. Participants were presented with a small white fixation point before the start of each trial. It remained on the screen until the participant started the trial by

pressing the space bar. At the beginning of the trial participants were presented with a red fixation point for 2000ms. They were instructed to maintain fixation and not blink during this time. Baseline pupil diameter was sampled during the last second of the red fixation. After the baseline measurement, the first stimulus was presented for 300ms followed by a small white fixation point for 500ms and finally the presentation of the second stimulus for 300ms. Participants were asked to compare the relative orientations of the reference and probe, pressing a left button to indicate that the second stimulus was rotated CCW from the orientation of the first, or a right button to indicate that the second was rotated CW from the first. After they pressed the response key, the white fixation point returned to the screen and participants advanced to the next trial by pressing the space bar.

The orientation of the probe was determined using the method of constants. The probe was oriented in one of seven directions between 30 and 60 degrees (30, 35, 40, 45, 50, 55, or 60 degrees, which spanned a range around the 45 degree reference orientation). Each probe orientation was presented 20 times for each surround condition. This led to 420 trials which took participants approximately 45 minutes to complete. Before beginning the experiment, participants completed 6 practice trials with various center and surround configurations. During the practice trials the stimuli remained on the screen for 500ms, instead of 300ms, to give the participants the opportunity to learn the task.

Analysis

Trials were categorized based on the baseline pupil size of that trial. For each participant and each condition, we categorized trials of “large” and “small” pupil size

using a median split. We calculated the orientation sensitivity and effect of the 15-degree surround for each of these trial cases. The effect of the 15-degree surround was determined by identifying the difference between the PSE for the CW and CCW surrounds and dividing by two. We determined the PSE for each condition by using a psychometric function to fit the probability that participants would perceive each probe orientation as tilted CW. Then we selected the orientation at which the function crossed the 50% point as the PSE.

Orientation threshold was determined by subtracting the point at which participants reported the orientation of the stimulus to be CW of the 45 degree reference orientation in 70% of trials from 45. Orientation sensitivity was calculated by taking the absolute value of the inverse of the orientation threshold. These values were calculated separately for each participant. We removed one participant because their orientation sensitivity in one condition was over 10x the average orientation sensitivity.

Results

In this experiment the 15-degree surround led to a significant repulsive effect (mean = 5.15 degrees, SD = 0.99, $t(29)=33.44$, $p<.01$). This effect is similar in magnitude to the effect we observed in Chapter 2, Experiment 1. When calculated using trials where the pupil was large, the mean effect was 5.21 degrees (SD = 0.86, $t(29)=33.26$, $p<.01$). When calculated using trials where the pupil was small the mean effect was 5.09 (SD = 1.11, $t(29)=25.07$, $p<.01$). These effect sizes were not significantly different from each other ($t(29) = 0.67$, $p=.51$; Figure 36)

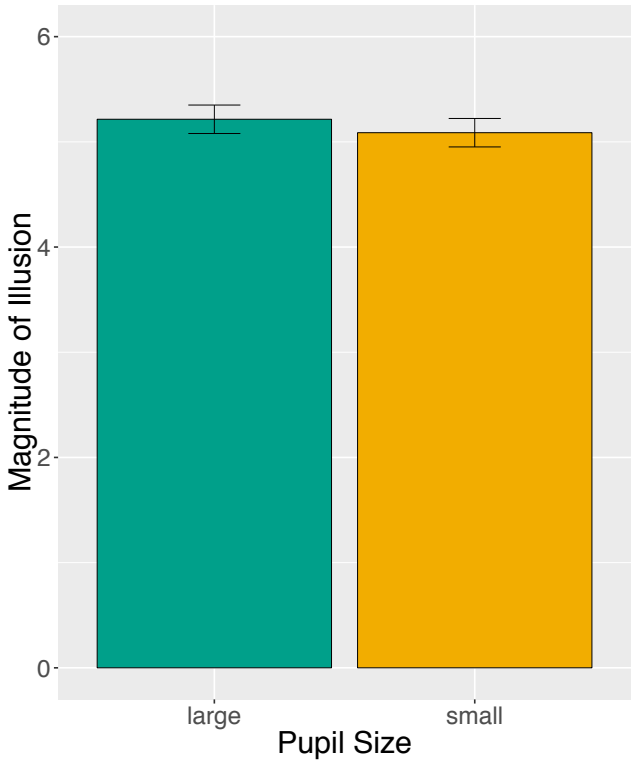

Figure 36. The magnitude of the illusion when calculated using trials where the pupil diameter was large or smaller within a participant. Error bars indicate within subject standard error.

The average orientation sensitivity was 0.79 degrees^{-1}. When calculated using trials where the pupil was large, the mean sensitivity was 0.91 degrees^{-1}. When calculated using trials where the pupil was small the mean sensitivity was 0.66 degrees^{-1}. While the means differed in the predicted direction (moderate arousal was associated with greater sensitivity), the difference was not significant (SD_{large} = 1.15, SD_{small} = 1.00, $t(29) = -1.03$, p=.31; Figure 37).

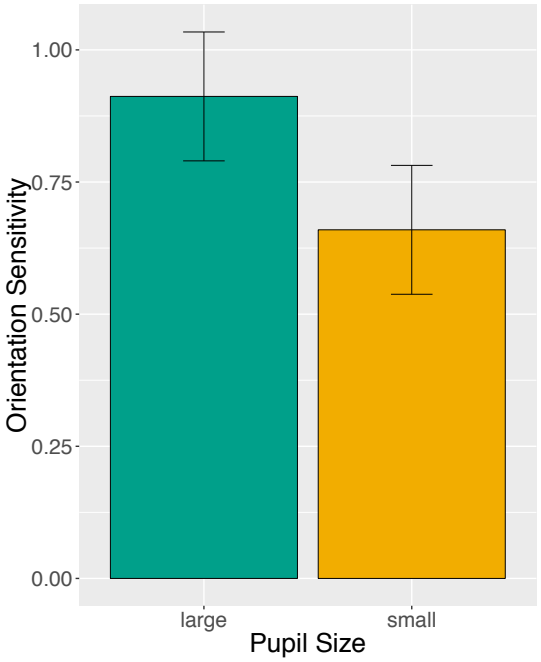

Figure 37. Orientation sensitivity when calculated using trials where the pupil diameter was large or smaller within a participant. Error bars indicate within subject standard error.

We ran a correlation to determine the relationship between the effect of the surround and orientation sensitivity. There was no significant correlation between the effect of the surround and orientation sensitivity ($r(28)=.07$, $p=.7$). Both the correlations between orientation sensitivity and the surround effect with large pupil trials ($r(28)=-.14$, $p=.45$) and the small pupil trials ($r(28)=.18$, $p=.33$) were not significant.

Discussion

In this study we tested the effects of natural fluctuations in arousal level on spatial integration and orientation sensitivity. We had predicted that internal changes to brain state alter the gain control on sensory responses and impact the

normalizing effect of the surround, leading to reduced perceptual repulsion and enhanced sensitivity.

Previous studies on humans (Bullock et al., 2017) and mice (Reimer et al., 2014; McGinley et al., 2015) have shown a neural enhancement associated with arousal. However, it is possible that neural enhancement from arousal leads to contrast detection sensitivity but not to orientation sensitivity. Previous work has shown no selective enhancement of sensory responses during locomotion (Fu et al., 2014; Niell & Stryker, 2010). Reimer et al. (2014) found that responses to all orientations were enhanced when mice were running but that orientation tuning was enhanced in mice V1 neurons during periods of pupil dilation. Therefore, we may expect to see changes to orientation sensitivity using pupil indicators but not locomotion indicators. However, when we compared the orientation sensitivity derived from trials that were split according to pupil size, there was no significant difference.

We also measured how arousal state impacts perceptual repulsion. We found that the 15-degree surround led to a repulsive effect that was similar in magnitude to the repulsive effect we observed in Chapter 2, Experiment 1. When we compared the effect size derived from trials that were split according to pupil size, there was no significant difference. This evidence would indicate that natural fluctuations in arousal do no modulate surround integration. This is not consistent with the neural effects measured in mice that show that surround suppression is reduced during times of locomotion (Ayaz et al., 2013).

The changes to neural response gain control during periods of pupil dilation and during periods of locomotion may be from two distinct mechanisms. The proposed mechanism of sensory response enhancement during locomotion is that nicotinic inputs from the basal forebrain activate VIP+ neurons in mouse V1 (Fu et al., 2014). This determines how gain control changes with behavioral states. The mechanism for selective enhancement responses to preferred orientation during pupil dilation is not clear. While pupil dilation is related to changes in LC-NE activity (Aston-Jones & Cohen, 2005) it is also impacted by many other factors.

Although we controlled for luminance, there are other internal cognitive processes/states that would lead to pupil fluctuations. For example, if someone is not paying attention to the task and is mind-wandering, their baseline pupil size may reflect what ever it is that they are thinking about but their performance is affected by the lack of attention on the task (Unsworth & Robison, 2018). This type of noise makes it very difficult to extract trials when the subject is attentive to the task and in a state of moderate arousal verses inattentive to the task and in a state of moderate arousal. Later we describe a future study that would be able to possibly account for some of this noise by measuring within-subject variability.

Another reason why arousal modulated surround integration might be observed in mice but not humans is that a reduction in arousal-modulated neural surround suppression may not lead to a reduction in perceptual repulsion. Ayaz et al. (2013) found that locomotion increased the driving response to the center stimulus as well as decreasing the suppressive input from the surround for stimuli that were essentially iso-oriented centers and surrounds. It is possible that arousal

raises the threshold required to activate inhibitory input from the surround, increasing the summation area. In other words, a neuron would need stronger suppressive input to show surround suppression. Because our stimuli were very large and with a high contrast, we may be unable to detect the small changes to neural summation in participants' perceptual reports. However, this seems like an unlikely reason to see null results since we are able to see the effects of neural surround suppression manifest as perceptual repulsion.

Unfortunately, we were not able to look at sensitivity and surround effects on a trial-by-trial basis using the categorical judgments of the current paradigm, since the quantification of these measures was only possible through the calculation of the full psychometric function. Therefore, in a future experiment we will have participants adjust a stimulus to match the perceived orientation of the center stimulus in the STI. The effect of the surround will be defined *in each trial* as the difference between participants' response and the actual orientation of the central probe. Not only will this allow us to look at changes in effect size on a trial by trial basis, but fewer trials will be needed, allowing for a shorter experiment time.

Future studies will also make use of an alerting tone on some trials as a way of directly modulating arousal. There is evidence that a brief 80Hz tone will elicit an increase in arousal and pupil diameter (Petersen, Petersen, Bundesen, Vangkilde & Habekost, 2017). In a small pilot study of 4 participants, we observed a 0.7 degree reduction in the magnitude of the illusion during trials when a tone was presented ($t(4)=1.63$, $p=.09$). We also observed a non-significant increase in orientation sensitivity on tone trials ($t(4)=0.68$, $p=.27$).

Finally, there was no correlation between orientation sensitivity and the magnitude of the surround effect. Previous research (Song et al., 2013), and the results from Chapter 2, Experiment 1, have found that the 15-degree surround effect decreases as orientation sensitivity increases. According to Song et al.'s (2013) results we should have had enough power to detect this relationship. However, our results from Chapter 2, Experiment 1 indicate that this effect may not be as robust as previously thought. This will be considered more in Chapter 5.

Conclusions

Counter to the findings in previous literature (Bullock et al., 2017; Reimer et al., 2014; McGinley et al., 2015), our results indicate that there is no enhancement to orientation sensitivity with increased arousal. We also found that surround effects are not reduced during states of higher arousal as indexed by pupil diameter. This is inconsistent with the results from a mouse study that found that surround suppression was reduced with arousal (Ayaz et al., 2013). Until we see a clear reduction in surround integration associated with behavioral or internal states of arousal in humans there will be a very important piece missing between the human and animal models of spatial integration. More work is needed to verify these results or to identify a method to optimally measure this modulation in humans. We suspect that we may be able to observe an effect using a different paradigm that allows for measuring effects on a trial by trial basis and for experimentally inducing arousal with the presentation of a tone.

CHAPTER 5: GENERAL DISCUSSION

The goal of this work was to provide insight into the perceptual processes and types of neural connections involved with spatial integration. Spatial integration can be studied using perceptual illusions that occur when the area around a target biases perception of that target. The influence of the surrounding area on the perception of a target's orientation is well established using the STI (Clifford, 2014; Gibson & Radner, 1937; Westheimer, 1990). The strongest repulsive effect happens where the difference between the angle of the center and surround is 10-20 degrees. The strongest attractive effect, a bias towards the orientation of the surround, occurs when there is a relative difference of 75-80 degrees.

In three studies we used psychophysical methods with versions of the STI paradigm to study how the visual system integrates information over space. We determined the extent to which prior experience with scene statistics impacts regional integration based on the probability that those regions are statistically dependent. Next we addressed the role of individual differences in autistic traits on spatial integration as a way to understand potential differences in connectivity and computation in the brains of people with autism. Finally, we aimed to determine the extent to which arousal states modulate spatial integration.

In our first study, we determined the extent to which different surround regions were integrated. A model of divisive normalization can act as a framework for making predictions about how the visual system will integrate information under various stimulus configurations. A flexible model of divisive normalization

accounts for cases in which the center and surround are part of the same object and cases when they are parts of different objects. When regions are co-assigned to the same object the center and surround activations will be dependent. The center is only normalized by the surround when they are co-assigned to the same object (Coen-Cagli, Dayan & Schwartz, 2012; Schwartz et al., 2009). The cortical output of the model is a Bayesian estimate of the local distributions given the dependencies between them.

Center and surround units tuned to natural scene statistics are more likely to be dependent when the surrounds are positioned collinearly to the center stimulus than when the surrounds are positioned laterally (Coen-Cagli, Dayan & Schwartz, 2012). We tested the extent to which the collinear and lateral regions of the full surround STI stimulus contribute to the overall surround effect. We predicted that the collinear region would drive the full surround effect for both perceptual repulsion (i.e. 15 degree surround) and perceptual attraction (i.e. 75 degree surround).

We found that the full 15-degree surround had the largest repulsive effect, followed by the collinear 15-degree surround, and the lateral 15-degree surround had the smallest effect. The full 15-degree surround effect can be thought of as a sum of the regional surround effects, weighted by the probability of dependency on the center. Contrary to our predictions, we found that the largest attractive effect came from the lateral 75-degree surround. The 75-degree collinear and full surround effects were smaller and not significantly different from each other. Furthermore, neither of the regional surround effects predicted the 75-degree full

surround effect. Attractive effects only manifest when the surround stimulus weakly normalizes the response to the center. While this effect is seen in the full surround configuration, it is possible that it is simply optimized when the surround is less likely to be dependent on the center (i.e. when the surround regions are lateral to the center stimulus).

Together, the results from these experiments indicate that the prior probability of dependency interacts with the strength of the stimulus input. The largest repulsive effect happens when strong stimulation normalizes the center response. The largest attractive effect happens when the stimulus input strength and prior probability of co-assignment are weak. The overall effect is a sum of the regional effects weighted by their dependency to the center. These results are consistent with a system that uses prior experience with natural scene statistics to integrate regions of space. This Bayesian estimate of the response distribution may be an efficient way for the visual system to represent information (Schwartz et al., 2006).

We also addressed potential differences in the regional integration mechanisms by measuring the relationship between effect size and orientation sensitivity, which may be an indicator of horizontal connectivity (Song et al., 2013; 2013b). Horizontal connectivity between the center and surround may vary with surround regions. Lacaruso, Gasler and Hofer (2017) found that there is more connectivity between receptive fields that are co-axially aligned and co-oriented to the center receptive field. Laterally aligned receptive fields had fewer connections to the center receptive field and the number of connections did not depend on

orientation preference. This demonstrates increased connectivity between receptive fields representing regions of space that have a higher probability of being co-oriented and, therefore, part of the same edge. Therefore, we predicted that orientation sensitivity would be most strongly correlated with the collinear surround effects of the tilt illusion.

We found that orientation sensitivity increased with the magnitude of the illusion from all 15-degree surround configurations. This indicates that the repulsive effects are all dependent on horizontal connectivity. However, there is evidence that the effect of the 15-degree lateral surround is more dependent on horizontal connectivity than the 15-degree collinear surround. The relationship with sensitivity is stronger for the lateral surround than the collinear surround. In fact, the relationship between sensitivity and the effect of the collinear surround did not appear in the early stages of data analysis with fewer than 100 participants. This is evidence that the repulsive effect of the collinear surround may be a product of two mechanisms: one that is dependent and one independent of horizontal connections in V1. It is possible that there is additional information about the probability of dependency between the center and surround that is fed back into V1 to modulate the magnitude of the effect.

There was no significant correlation between orientation sensitivity and the effect of any of the 75-degree surrounds. This could indicate that the 75-degree surround effects are not as dependent on the limitations of horizontal connectivity or possibly that individual difference in the attractive effects rely more on other types of connections, such as feedback or local inhibitory connections. Although

some researchers have suggested that the attractive effects stem from feedback (Smith and Wenderoth, 1999; Wenderoth & Johnstone, 1988), it is unlikely that the attractive effects rely solely on feedback connections (Kim and Freeman, 2014). Attractive effects are also thought to arise from the disinhibition of local inhibitory connection (Dragoi & Sur, 2000). Only using observations from the first study it is unclear if individual differences in the attractive effects would be related to feedback or local inhibitory connections.

In our second study, we determined the extent to which autistic traits are associated with changes in orientation sensitivity and spatial integration. This has potential implications for understanding changes to integration mechanisms in disorders that have disrupted perception. It is thought that an elevated ratio of excitatory to inhibitory responses would lead to some of the social and perceptual impairments seen in autism (Rubenstein & Merzenich, 2003) and this has been modeled with divisive normalization (Rosenberg, Patterson, & Angelaki, 2015). However, Van de Cruys et al. (2018) found that there was no difference between tilt illusions in participants diagnosed with ASD and neurotypical controls for a cross orientation suppression task. The authors argued that this was evidence that people with ASD do not show decreased normalization in low-level perception. However, it is still possible that a flexible model of normalization could account for perceptual differences in ASD. We explored this by looking at the relationship between autistic traits and regional surround integration in neurotypical participants. Autistic traits have been found to exist as a continuum in the general population (Baron-Cohen et al., 2001). Previous research has demonstrated that people who score high on AQ

have reduced surround suppression (Flevaris & Murray, 2015). We predicted that people who score high on autism traits would have reduced surround effects for all surround types, consistent with a general model of decreased normalization.

There was no clear relationship between repulsive surround effects and autistic traits. Although none of these effects were significant in Experiment 1, the means were trending in the predicted direction: people who scored high on AQ and SQ-R showed overall lower repulsive effects of the surround. We observed a negative correlation between IS and the 75 degree lateral surround effect. That is, people who scored high on IS had larger lateral attractive effects. This subscale has been associated with local contrast effects (Reed & Dassonville, In Progress). It is possible that IS measures a trait that is related to the attractive component of spatial integration and that is only apparent when the repulsive component has been removed. This does not appear to be related to horizontal connectivity. Attractive effects of the tilt illusion are thought to arise from disinhibition. Our results suggest that the relationship between IS and local context effects includes (and may be specific to) local disinhibition.

We did not find evidence for a general reduction in normalization for people who scored high on autistic traits. Our results would also suggest that there is no reduction in normalization in a flexible model tuned to natural scene statistics. Van de Cruys et al. (2018) proposed that people with autism may still rely on prior experience with natural scenes but that their use of the prior may be delayed. In fact, a meta-analysis showed that people with autism process global information more slowly than neurotypical controls (Van der Hallen et al., 2015). Therefore, we

would expect that people with autism (or neurotypical participants that score high on autistic traits) would show a delayed effect of the collinear surround. This would be an excellent area to follow up with future studies.

There is evidence that people who score high on AQ show decreased surround suppression (Flevaris & Murray, 2015) and increased orientation sensitivity (Dickinson, Jones & Milne, 2014). If the relationship between sensitivity and context effects for people who score high on AQ is due to a lower level of horizontal connectivity then we would predict that AQ would fully account for the relationship between sensitivity and context effects. Our results indicate that these relationships are not as robust as previously indicated and that there is not a single autistic trait to relate the correlation between sensitivity and context effects.

In Experiment 1 we found a trend that people who score high on SQ-R have higher orientation sensitivity but this result was not replicated in Experiment 2 (although the means we were in same direction). When we pooled the participants from Experiment 1 and Experiment 2 we had enough power to detect a small effect of AT on orientation sensitivity. However, this effect disappeared when we accounted for sex differences. Males had higher orientation sensitivity than females, which is consistent with previous work showing males are have smaller motion detection thresholds (Murray et al., 2018). Importantly, pooling the participants from each experiment provided enough power to increase our confidence in the null relationship between autistic traits and sensitivity. The relationship between sensitivity and autism has been inconsistently observed in the previous literature (Shafai, Armstrong, Iarocci & Oruc, 2015).

It is worth mentioning that the mean orientation sensitivity appears to be higher for people who score high on AT but lower for people who score high on IS. Mean repulsive surround effects were lower for participants who scored high on AT, but higher for participants who scored high on IS. These relationships with were non-significant but demonstrate that the SQ-R subscales may be measuring different individual traits that are related to low-level vision.

In our third study we determined the extent to which spatial integration is modulated by natural fluctuations in internal arousal states. Here, we measured the amount of perceptual repulsion caused by an oriented surround for cases of low and moderate arousal, as indexed by pupil size. It has also been shown that arousal increases neural sensitivity (Reimer et al., 2014; McGinley et al., 2015) and reduces surround suppression (Ayaz et al., 2013) in animal studies. While the effects of arousal on visual processing is quite convincing in animal studies, it is less convincing in humans (Benjamin et al., 2018; Bullock et al., 2017; Kim et al., 2017). There is no evidence that surround suppression decreases with moderate arousal in humans.

Pupil dilation has been used, in humans (Gilzenrat et al., 2010) and animals (McGinley et al., 2015; Reimer et al., 2014), as an indicator of arousal responses. We predicted that there would be an increase in orientation sensitivity when the participants' pupils were large. We did not observe a significant difference in perceptual orientation sensitivity at different arousal states which is inconsistent with previous literature showing neural response enhancement (Bullock et al., 2017; Reimer et al., 2014; McGinley et al., 2015). We predicted that the magnitude of

the orientation illusion would be largest when the participant was in a state of low arousal and smallest when the participant is in a state of moderate arousal. There was no significant difference between the surround effects derived from trials when the pupil was small and trials when the pupil was large. This suggests that natural fluctuations in arousal, as indexed by pupil dilation, do not modulate surround integration. It could also indicate that natural fluctuations in arousal during the task were too small to influence surround repulsion.

In future studies this could be addressed with a phasic auditory altering paradigm to induce arousal on specific trials (i.e., boost arousal with the presentation of a tone). In a small pilot study we observed a 0.7 degree reduction in the magnitude of the illusion and a non-significant increase in orientation sensitivity on trials when a tone was presented. Future studies will also use an adjustment task so that we can look at how surround effects are predicted by pupil dilation or tone on a given trial. Until we see a clear reduction in surround integration associated with behavioral or internal states of arousal in humans there will be a very important piece missing to connect human and animal models of spatial integration.

The results from these three studies inform our understanding of the biological and cognitive processes involved with spatial integration. From the behavioral results we are able to make some inferences about the mechanisms involved. The repulsive surround effects seem to be driven by orientation specific horizontal connections that act through divisive normalization. Feedback connections may augment the magnitude of this normalization by providing information about the probability of dependency between center and surround

stimuli. The attractive effects occur only when the horizontal inputs are weak and the feedback is weak or non-existent. Disinihibition from local connections causes the normalization to have a facilitative effect.

It is unclear if these results can inform our understanding of autism or other disorders that have disrupted perceptual processing. At this point it appears to support the finding that autism is not associated with decreased normalization (Van de Cruys et al., 2018). We were not able to determine if autistic traits accounted for differences in horizontal connectivity. However, there is some evidence that Insistence on Sameness, a subscale of the SQ-R, is related to increased disinhibition or excitatory responses.

These studies also provide us with valuable information about the behavioral methods used to study spatial integration. We used the correlation between orientation sensitivity and the magnitude of the STI as an indicator of dependence on horizontal connectivity. While previous research has shown that this is a very robust correlation (Song et al., 2013), our results demonstrate that it is not as large or consistent of an effect as previously thought. When the relationship was clear in Chapter 2, Experiment 1, the correlation was not as strong as we expected it would be with over 100 participants. Furthermore, our analysis shows that adding sensitivity does not predict the full surround effect when the regional effects are predictors. Our control experiment in Chapter 2, and the experiment in Chapter 4, each with 30 participants, did not show the relationship between orientation sensitivity and the repulsive surround effect.

We also demonstrate that more work is needed before we have a paradigm where we can predict spatial integration effects using pupillometry. This is important to pursue as an inexpensive and non-invasive measure. Despite a promising step forward, there are still several questions left unanswered or unclear. Future studies will include 1) adaptation to the pupillometry paradigm, 2) exploring the difference between induced and natural fluctuations in arousal, and 3) using stimulus timing as a way to understand the onset of horizontal and feedback driven effects and how that onset varies with autistic traits.

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